

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 04 October 2017

Wellington House, Waterloo Road, London

Members

Professor Andrew Pollard (Chair)
Dr Andrew Riordan (Deputy Chair)
Prof Anthony Harnden (Deputy Chair)
Prof Judith Breuer
Prof Matt Keeling
Dr Fiona van der Klis
Alison Lawrence

Prof Adam Finn
Prof Rob Read
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 Jonathan Van-Tam (DCMO)

Secretariat

Andrew Earnshaw
Ruth Parry
Jonathan Crofts

Dr Mary Ramsay
Dr Gayatri Amirthalingam

Invited Speakers

Dr Richard Pebody (PHE)
Dr Mark Jit (PHE)
Dr Shamez Ladhani (PHE)
Chris Mullin

Prof David Goldblatt (UCL)
Prof Nick Andrews (PHE)
Dr Yoon Choi (PHE)

Invited observers from Devolved Administrations

Dr Anne Kilgallen (DHSSNI)
Dr Syed Ahmed (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 (NaTHNaC)
Dr Darina O'Flanagan (Eire)
Dr Dipti Patel (NaTHNaC)
Dr Michael Edelstein (PHE)

Dr Vanessa Saliba (PHE)
Ruth Howlett-Shipley (MoD)
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. The Chair asked members to provide an update about any declarations of interest, following the review of declarations undertaken prior to the meeting by the secretariat. Declarations of interest were duly updated.
3. The Chair welcomed Prof Jonathan Van-Tam to the meeting who had recently been appointed as Deputy Chief Medical Officer at the Department of Health.

I. Minute of the June 2017 meeting

4. The Minutes of the June 2017 meeting were agreed without change

II. Matters arising

Research prioritisation process

5. The Committee noted that the secretariat and the Deputy Chairs had worked to develop a process for recording and prioritising research advised by the Committee and sub-committees. This would be important in providing the Committee's advice on research to the Advisory Group on Vaccine Evaluation Research, which would oversee the work of the National Immunisation Schedule Evaluation Consortium (NISEC). The priorities would also be placed in the public domain for use by academic and other groups.
6. The Committee noted work currently planned by NISEC. It was considered important to specify that the Committee would only be identifying research needed and prioritising, and would not be involved in funding or commissioning any trials. The Committee agreed the work was important to ensure research was undertaken in a timely manner to ensure the necessary evidence was available for the provision of advice. The Deputy Chairs agreed to update the priorities and circulate to members for comment.

Action – Deputy Chairs to update and circulate the research priorities to members for comment.

III. Cost-effectiveness Methodology for Immunisation Programmes and Procurement

7. The Committee noted that in 2013 the Committee had suggested that a working group be established to examine the question of how the impact of vaccination programmes to prevent rare diseases of high severity could best be assessed

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and whether there were aspects of cost-effectiveness in relation specifically to children and to vaccines that should be considered.

8. In 2014 the Department of Health commissioned a working group to examine this issue – the Cost-Effectiveness Methodology for Immunisation Programmes and Procurement working group (CEMIPP). CEMIPP reported its findings to the Department on 20 July 2016. Most recently the Appraisal Alignment Working Group (AAWG) within DH had been asked to consider the report. The Chief Economist at DH was asked to provide an update to the Committee.
9. The Committee noted the new Minister for Public Health and Primary Care had a lot of very technical information to consider, in terms of the CEMIPP report, and that the Department's Appraisal Alignment Working Group (AAWG) had been asked to provide Ministers with advice on the conclusions of the report. The AAWG had been considering the latest evidence on the marginal cost of a QALY in the NHS, looking at examples of how the recommendations would affect the cost-effectiveness of vaccines, and considering the wider context across the health system. AAWG planned to provide their advice to Ministers towards the end of 2017.
10. The Committee thanked the Chief Economist (Chair of the AAWG) for the update, and asked that he return in February to provide an update following submission of the AAWG advice to Ministers.

IV. Pneumococcal vaccination

Epidemiology of pneumococcal disease

11. The Committee noted a presentation from Public Health England (PHE) on the epidemiology of pneumococcal disease in England and Wales. The Committee noted that:
 - an overall 37% reduction in invasive pneumococcal disease (IPD) incidence since the introduction of PCV7;
 - a further 7% reduction since the introduction of PCV13;
 - PCV13 serotypes were responsible for 19% of IPD cases overall, mostly in adults aged >15 years (96%);
 - these cases were mainly serotypes 3 (49%) & 19A (29%);
 - serotype 3 IPD continued to increase, especially in adults and older adults;
 - serotype 19A IPD rates were fluctuating, also in adults and older adults;
 - PCV13 serotypes were now rare in children, accounting for around 10% of IPD cases in children under 2 years of age; with serotypes 3 and 19A being responsible for nearly all cases
 - it was estimated that almost 40,000 cases of IPD had been prevented since the start of the PCV programme; and
 - the case fatality rate for IPD had reduced from the pre-PCV era.

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Immunogenicity of PCV13 delivered with one primary and one booster dose (1+1) in UK infants

12. The Committee noted a presentation from Prof David Goldblatt lead investigator on the National Vaccine Evaluation Consortium (NVEC) study into the immunogenicity of an alternate pneumococcal conjugate vaccine schedule in infants. The Committee noted that:

- infants either received doses of PCV13 at 2m, 4m and 12m (2+1), or at 3m and 12m (1+1), alongside other vaccines according to the routine schedule;
- blood samples were taken at 5m and 13m, with nasopharyngeal swabs taken at 12m and 18m;
- immunogenicity of a 1+1 schedule was equivalent to, or superior to, a 2+1 schedule for 9 of the 13 serotypes in PCV13;
- almost all infants in both the 1+1 and 2+1 schedules had IgG above the protective titre of 0.35µl/ml, for all serotypes except serotype 3, for which fewer vaccinated infants reached protective thresholds in both schedules;
- geometric mean concentrations following the primary series were higher in the 2+1 schedule; and
- in particular, both the geometric mean concentrations and proportion of infants protected against serotype 19A were similar between the two schedules.

Pneumococcal carriage study 2015/16

13. The Committee noted a presentation from PHE on the Pneumococcal Carriage Study undertaken in 2015/16, noting that:

- between 2012/13 and 2015/16 there had been an overall significant increase in the non-vaccine type case:carrier ratio from 10.9 to 16.8 cases/100,000 carriers;
- in terms of circulating non-vaccine serotypes, the UK was at the time of the 2015/16 survey still in a state of flux, with changes leading to a rise of non-PCV13 serotypes with an increased case:carrier ratio;
- carriage of serotype 6C had significantly reduced between 2012/13 and 2015/16, consistent with cross protection from the 6A component of PCV13;
- although overall carriage prevalence was similar between surveys, there had also been a small overall rise in carriage of non-PCV13 serotypes (consistent with an increased force of infection); and
- low levels of serotypes 3 and 19A remained in circulation in the population.

Modelling the impact of changing to a PCV13 1+1 schedule

14. The Committee noted a presentation from PHE on modelling on the potential impact of moving to a 1+1 schedule for PCV13 in the UK. The Committee noted that:

- the main aim of the model was to investigate potential causes of the unexpected increase among non-PCV13 serotype IPD cases since 2014/15

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and;

- to compare the long-term impact in the UK of -
 - continuing with a 2+1 schedule;
 - changing to 1+1 schedule in 2018;
 - stopping the PCV13 programme in 2018;
- carriage rates were based on a 2001/02 longitudinal pre-PCV7 carriage study;
- pre-PCV7 IPD cases and carriage were used for estimation of case-carrier ratios, but this was allowed to change to a new level for non-PCV13 serotypes from 2014/15 along with the NVT force of infection;
- post- PCV7 IPD cases from 2005/06 to 2015/16 were used for model fitting, adjusted for surveillance improvements prior to 2010;
- PCV vaccine coverage was based on General Practice Research Database (GPRD) data for the first two years after PCV7 introduction, to capture the PCV7 catch-up cohort;
- routine coverage of primary and booster doses was assumed to continue at the same level;
- contact patterns were based on the POLYMOD study and infant contact survey by van Hoek *et al.* (2013);
- contact patterns were adjusted for demographic changes in the population;
- serotype 1 had been excluded from the study as its behaviour was inconsistent with model predictions, with cases declining after PCV7 introduction; its exclusion would have little impact on predicting the long term impact of the PCV13 programme due to the current low level of cases due to serotype 1.
- serotype 3 was treated as a non-vaccine serotype because of data showing lack of effectiveness or population impact after PCV13 introduction;
- vaccine efficacy against carriage was estimated by fitting to post-PCV IPD data;
- waning of vaccine efficacy against carriage was estimated from fitting the model to US IPD data after PCV7 introduction by Melegaro *et al.* (2010);
- an assumption was made that a single dose infant programme would provide half the protection against carriage of two doses or a booster dose, and would wane more rapidly;
- protection against carriage was assumed to be the same after the booster dose irrespective of the number of priming doses; and
- vaccine protection against IPD was assumed to wane more rapidly with one infant dose than two doses or a booster dose.

15. The results included the following:

- The best fitting model indicated a modest increase in the case:carrier ratio and force of infection, consistent with the results of the carriage study;
- despite more aggressive serotype replacement than initially predicted, if the increased force of infection and case-carrier ratio persisted, then there would still be a long-term reduction in overall IPD cases compared with the pre-PCV7 era; the model also predicted that the increase in non-vaccine types would plateau in about 2 years;
- moving to a 1+1 schedule might increase IPD cases in infants because of

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loss of direct protection and in older adults because of a reduction in herd immunity as a result of less protection against carriage in infants after a single dose;

- an alternative 'simple calculation' method using vaccine effectiveness estimates, coverage data and the current incidence of vaccine-type IPD was also used to estimate any excess in infant cases that may occur due to the loss of direct protection in the first year of life; and
- both estimates indicated that any excess cases in infants or the older age groups would be very small following a move to a 1+1 schedule in the UK.

Discussion

16. The Committee agreed with the conclusions presented, that there had been significant reductions in vaccine-type disease in all age groups since the introduction of pneumococcal conjugate vaccines into the childhood programme, and that the booster dose was thought to be critical for ongoing control of vaccine-type IPD. Data from the clinical trial of a 1+1 schedule indicated that the post-booster responses were preserved for most serotypes, especially serotype 19A, and the carriage study indicated that carriage of vaccine serotypes was very low. Modelling indicated that a move to a 1+1 schedule might lead to a limited increase in cases of IPD, with very few of those being in young children. The Committee agreed that the modelling had been parameterised well.
17. Members commented on the fact that the current infant schedule was very busy, with some appointments having four vaccines at a single visit, and a move to a single dose at three months of age would ease pressure on the schedule, with up to 800,000 fewer doses administered annually. The Committee also agreed that the major benefit from the programme was being achieved through the booster dose at 12 months of age. The possibility of a partial implementation was considered which would allow for a control group to be monitored for secular trends during the implementation period; however, this was not considered further. The possibility of a carriage study coincidental with a move to 1+1 was discussed; however, the group considered that this would be difficult given the small numbers of carriers of the vaccine serotypes, which would require a very large carriage study to obtain sufficient power to detect significant differences.
18. The Committee agreed that any move to a 1+1 schedule would require maintenance of the high quality surveillance for pneumococcal disease currently in place in the UK, to ensure any changes in disease epidemiology were accurately captured in a timely manner.
19. The Committee agreed that the advice was provided on provisional basis, since the UK would be the first jurisdiction to use this approach, and would be reviewed closely by the Committee to regularly assess the impact of the change.

Conclusions

20. The Committee agreed that the PCV programme in the UK had been highly successful, with large and sustained decreases in PCV13 serotype disease across the population. High vaccine uptake in the UK combined with good

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vaccine effectiveness provided the UK with an opportunity to move to an alternate schedule. Given the success of the programme, both in those vaccinated, and the wider population through indirect population protection, the Committee agreed that a move to a 1+1 schedule was appropriate for the UK situation. The Committee, therefore, advised a revised schedule for PCV13 vaccine, with vaccination offered at 3m and 12m.

21. The Committee re-emphasized the need for continuing high quality surveillance to identify any change in case numbers. PHE noted the advice of the Committee and indicated they would begin discussions with the manufacturers on the timing of implementation.

V. HPV vaccination for adolescent boys

Report from the chair of the HPV subcommittee

22. The Committee received an update from the Chair of the HPV sub-committee on the outcome of the September 2017 sub-committee meeting held via teleconference. The sub-committee had considered the response from stakeholders to JCVI's interim advice and an update from the PHE impact and cost effectiveness modelling.
23. A common theme raised by stakeholders was that the interim statement did not provide enough information about the modelling work by PHE and Warwick and that this should be made publicly available. It was not possible at this stage to share the work fully for reasons of academic confidentiality as both pieces of work were intended for publication. Even more importantly, PHE still had to conduct final checks on the current results and JCVI had not completed its process of reviewing the work by PHE, which still had to undergo independent peer review and as a result could be subject to further changes.
24. The Committee noted that PHE had met with HPV Action after the Subcommittee meeting to discuss its work and provide the stakeholder with the opportunity to ask questions. PHE had also indicated to the subcommittee that it would be willing to share more details on the methodology of the assessment on a pre-publication server once final reviews were completed. It was also noted that the University of Warwick work was close to being published and an earlier draft had been shared in confidence with HPV Action.
25. Equality was also a key theme highlighted by stakeholders as a reason why boys should be included for vaccination. The role of carrying out an equality analysis remained the responsibility of the Department of Health in the development of policy based on the advice of the Committee. The Committee noted an equality analysis was in development and the Department of Health had nothing further to report at this stage. The stakeholders had also raised some legal questions on the equality issue and whether it was discriminatory to conduct an incremental cost-effectiveness analysis of a boys programme on the current girls programme.
26. The stakeholders had also suggested the PHE estimates for the attributable fraction (AF) of HPV types causing oropharyngeal cancers were too low. PHE

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had outlined its data sources for this at the subcommittee meeting and subsequently also to HPV Action in a separate meeting. PHE agreed to present to JCVI a quick analysis of what proportion of the benefits from vaccination would be due to the prevention of oropharyngeal cancers and whether changing the AF would make a substantial difference to the overall conclusions.

27. The latest outputs from the PHE model showed that the cost-effectiveness of a boys programme had improved. However, at the current list price a programme would still clearly not be cost-effective. The sub-committee did not know what price was paid for the vaccine in the UK programme, and the results indicated that in the base case scenario there may be a much lower but positive price at which a programme could be cost-effective. The view was that the PHE findings were similar to the other models which gave a cost-effective price at or around zero. The latest results from PHE still required checking and the sub-committee recommended to JCVI that the PHE model be peer reviewed before making any final conclusions.
28. It was also noted that the modelling work had been a resource intensive exercise for PHE, diverting resources from other work. It would not be possible to continue much longer under current arrangements and additional resources needed to be identified for the work to be developed further. The Chair thanked the sub-committee Chair for the report.

PHE impact and cost-effectiveness assessment

29. The Committee noted that since June 2017 PHE had made some changes to the model and that there was now greater confidence in the results. However, as these results had been generated close to the meeting, PHE still needed to perform some checks to confirm the outputs. The changes included:
- that the model was now fitted to female DNA prevalence data only, as there were no good quality UK DNA prevalence data on males, and the general consensus was that seroprevalence was difficult to interpret and not a reliable indicator for males;
 - this meant that the transmission parameters in the model were now the same for males and females;
 - that to interpret sexual behaviour in the NATSAL data, a synthetic scenario had been created averaging the range of partnership scenarios previously used; and
 - the model fitting had been run for longer.
30. As a result, there were no longer extremely large outliers, and the model fit was improved. The rebound effect due to vaccine waning was much smaller and the outputs for anogenital warts were more reliable. The latest outputs indicated that with female only vaccination, vaccine-type warts would be expected to be eliminated in all heterosexuals, and with a gender neutral programme vaccine-type anal cancer might also be eliminated.
31. The preliminary results now indicated that there was a positive, albeit very low

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threshold price in the base case scenario, which also met the uncertainty criteria. Duration of protection remained an important issue in the modelling with the results more favourable in the sensitivity analysis of 20 years duration. In the base case lifelong protection was assumed. The exact tipping point where the duration of protection was virtually as good as lifelong protection was most likely between 20 and 30 years but this needed further investigation to be more certain.

32. The Committee noted that the main benefit of including boys' vaccination, according to the preliminary results, was due to the additional herd protection it provided to girls. Approximately half of the additional benefit from boys' vaccination came from preventing HPV-associated cancer in females. Of the remaining additional benefit, which was in males, just under half was accounted for by the prevention of disease in MSM.
33. The preliminary results from PHE also suggested that the additional benefit from a boys programme in preventing oropharyngeal cancer in males was less than 10% of the total additional benefit. The latter indicated that if the PHE estimate of the AF was doubled it would have a relatively small effect on the overall willingness to pay threshold price for the vaccine.
34. The Committee noted that duration of protection remained an important issue but agreed that, given immunogenicity data and findings from the clinical trials it was more plausible that the duration of protection was closer to, and as good as, lifelong protection than 20 years.
35. The Committee noted there was the potential for small changes which cumulatively might start taking the threshold price into the realms of cost-effectiveness at a realistic price. These changes could include a fall in coverage in a girls programme, using twenty years duration of protection, a very large increase in the attributable fraction of OPC caused by HPV, dramatic increases in HPV-related disease in the future, and use of the 9 valent vaccine. It was also noted that a 1.5% discount rate would also make a boys programme more cost-effective.
36. The Committee noted that the question had been raised on what the comparator should be in the cost-effectiveness assessment. There was also the question of whether an average vaccine price for a girls and boys programme should be considered rather than the price for the vaccine for boys determined by the incremental analysis. The Committee requested that DH consider these questions and report back to JCVI about what was appropriate. The Committee also noted that because there was more than one type of HPV vaccine available, there was the potential to consider using HPV vaccines of differing valences for girls and boys.

Action: Department of Health to consider the appropriateness of the comparator currently used and to report back to the Committee

37. The Committee agreed that given the latest findings it was important to be sure about the modelling results and that PHE would need to complete its checks to confirm the findings. It was also important, for JCVI to carry out its due diligence

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of the work before making its conclusions. Therefore the Committee agreed that the model needed to undergo independent peer review before it could finalise its recommendation. The Committee also noted that some additional work on sensitivity analysis had been suggested as well, and that PHE was exploring ways of finding the additional resources to carry out this work.

Conclusions

38. In conclusion the Committee thanked stakeholders for their helpful comments and agreed that a number of these should be taken into account or considered further. The Committee noted that the modelling work needed final checks, peer review and additional scenarios and sensitivity analyses explored. The equality analysis was not yet completed and the Committee asked the Department of Health to share key messages from early work on the equality analysis once completed. Questions had been raised on the rules used in the economic analysis, and the Committee asked the Department of Health and the secretariat to consider these further and report back with their conclusions. As a result of these outstanding issues the Committee agreed that it was not yet in a position to finalise its recommendation on boys' vaccination.

VI. Influenza vaccination

Epidemiology, uptake and vaccine effectiveness

39. The Committee noted that reports of an intense A(H3N2) influenza season in the southern hemisphere were generating concerns about the NHS's capacity to cope in the event of the UK experiencing a similar level of influenza activity due to A(H3N2) this winter.
40. The Committee noted that the A(H3N2) subclade C3.2a1 circulating in the southern hemisphere was the same as that which circulated in the UK last winter. The Committee noted that there was no clear pattern about the spread of influenza between the hemispheres and that the preceding southern hemisphere influenza season was not necessarily a predictor of what would follow in the subsequent UK winter.
41. The WHO had recently met to determine the influenza vaccine composition for the southern hemisphere 2018 season. The A(H3N2) component had been changed from A/Hong Kong/4801/2014 (H3N2)-like virus to A/Singapore/INFIMH-16-0019/2016. The Committee noted that the change to the A(H3N2) strain was mainly for manufacturing reasons as the new A(H3N2) vaccine strain had a very similar antigenic profile to the previous vaccine strain.
42. The Committee noted that influenza activity in the UK was currently very low. So far there was a good match to the 2017/18 vaccine strains for those viruses that had been detected and characterized to date, but it was not possible to predict what kind of forthcoming influenza season to expect.
43. PHE presented a review of the 2016/17 season, focusing on the reduced influenza vaccine effectiveness seen in the elderly. The Committee noted that

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vaccine uptake was high (70.5 %) in all those aged 65 years old and above with uptake highest (estimated to be 80%) in those aged 75 and older, with the majority of vaccinated individuals having previously received multiple prior vaccinations. In those elderly individuals recorded as unvaccinated in 2016/17 there was a much lower prior vaccine status.

44. A review of the recent UK surveillance data over the most recent five seasons showed similar or higher primary care consultation rates in those aged 65 to 74 years than in those aged 75 years and older, excepting the 2016/17 season.
45. Excess all-cause mortality estimates over the previous six seasons were higher in both the 65-74 year age group and 75 years upwards age groups during A(H3N2) seasons compared to A(H1N1)pdm09 seasons. The 75 years upwards age group had a much higher influenza attributable mortality rate reported, and were estimated to be approximately seven times more likely to die from influenza on average compared with those aged 65-74 years.
46. The Committee were reminded that VE estimates for the 2016/17 season showed significant effectiveness against all laboratory confirmed influenza and specifically the A(H3N2) virus in 18-64 year olds but non-significant VE in the 65 years upwards age group. A recently published meta-analysis of Test Negative Case Control studies from 2004 to 2015 (Belongia et al 2016) also showed similar results, with significant effectiveness against A(H3N2) in working age adults, but a non-significant VE in older adults.
47. PHE had conducted an analysis of pooled data since 2005/06 from primary care surveillance schemes stratified by 65-74, 75-84 and 85 years upwards age groups. This showed significant VE in the 65-74 age group for all influenza, A(H1N1)pdm09 and influenza B and evidence of protection against A(H3N2). Above the age of 75 years old, pooled estimates of VE across all seasons was non-significant against all the influenza virus types. The Committee noted that vaccine effectiveness against more severe endpoints would also be useful to see.

Alternative influenza vaccines

48. The Committee noted that an adjuvanted trivalent inactivated influenza vaccine (aTIV) that had been used for some time in other countries was now licensed in the UK for use in the elderly and available for GPs to order for the 2018/19 season. Another potential vaccine for the elderly, a high dose inactivated vaccine, currently licensed in the US, was unlikely to be licensed in the UK for the foreseeable future.
49. The Committee noted that the available evidence indicated better immunogenicity and effectiveness for aTIV in comparison with non-adjuvanted inactivated influenza vaccines (IIV) in the elderly. In a study undertaken in an elderly population where more than 50% were over the age of 85 years, aTIV showed a highly significant effectiveness and relative effectiveness compared with IIV, which showed no effectiveness (Van Buynder et al, Vaccine 2013). Data provided by the manufacturer showed that compared with TIV, aTIV demonstrated superior seroconversion rates in the elderly and superior geometric mean titres in

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clinical risk groups against all three influenza vaccine types. The MHRA also indicated there were no concerns about its safety.

Cost-effectiveness of adjuvanted trivalent influenza vaccine in the UK

50. The Committee received a presentation on assessing the impact and cost effectiveness of aTIV in the elderly. The Committee noted that the manufacturer had also undertaken a cost-effectiveness analysis of aTIV based on the PHE influenza transmission model structure but had used a higher VE estimate and higher costs for primary and secondary care compared with the PHE assessment. Both models indicated a programme in the 65 years upwards age group would be cost-effective at the list price of the vaccine.
51. PHE had also looked at the cost-effectiveness of an aTIV programme in the 75 years upwards age group compared with the current programme and then with the further addition of an aTIV programme in the 65-74 age group. The Committee noted that aTIV, under quite conservative estimates of effectiveness, would be highly cost-effective in both the 65-74 and 75 and over age groups.

Conclusions

52. The Committee agreed that the available evidence indicated adjuvanted influenza vaccines were more effective in those over 65 years of age, compared with influenza vaccine currently used in the UK. Mathematical modelling indicated that, under quite conservative estimates of effectiveness, the adjuvanted vaccine would be highly cost-effective in both the 65-75 and 75 and over age groups.
53. Given the low influenza vaccine effectiveness seen in the over 65-74 year olds over several A(H3N2) dominated seasons, and non-significant VE for all types of influenza in the over 75s, the Committee agreed that use of aTIV in those aged 65 years and over would be both more effective than the non adjuvanted vaccines currently in use, and also cost-effective.
54. The Committee agreed that if a change in approach were to be considered, switching vaccination of the 75 years and upwards age group to adjuvanted vaccine would be the first priority, given the un-adjuvanted inactivated vaccine showed no significant effectiveness in this group.
55. The Committee asked the Department of Health, Public Health England and NHS England to give consideration to the evidence that had been provided on the provision of adjuvanted influenza vaccine to those aged 65 years and over. The Committee recognised, however, that there were also practical issues for DH to consider for such a policy, because of the current arrangements for procurement for influenza vaccines for those aged 65 years upwards, which were procured by individual GPs and Clinical Commissioning Groups and open to market choice.

VII. Update from the Varicella sub-committee

56. The Committee noted a short update from the Chair of the Varicella sub-committee. The sub-committee had begun considerations on a new, non-live,

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herpes zoster (shingles) vaccine. Initial data had indicated very high vaccine efficacy with good duration of protection, and modelling indicated the vaccine was likely to be highly cost-effective. The sub-committee would consider updated modelling in 2018, and would be considering use of the vaccine in those contraindicated to live vaccines in the current routine programme, the additional willingness to pay for the new vaccine in the current programme at 70 years of age, and whether the characteristics of the vaccine led to differing conclusions on the optimal age for vaccination.

VIII. Papers for Comment

57. The Committee noted a retrospective case-control study in sexual health clinics in New Zealand, which indicated that the MeNZB vaccine had reduced rates of gonococcal disease in those vaccinated. As this vaccine had similarities to Bexsero®, the Committee agreed this would be of interest in future discussions on the cost-effectiveness of Bexsero in adolescents.

IX. Coverage

58. The Committee noted the latest data on immunisation coverage across the UK. Considerations were again made regarding the continuing trend for lower uptake of shingles vaccine in those eligible. The Committee noted concerns raised regarding efforts to campaign against specific vaccines, and how this could impact on vaccine coverage. The Committee were reassured that PHE and agencies in the devolved administrations were taking appropriate actions in this regard.

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Prof Andrew Pollard (Chair)
<p>Professor Pollard receives no personal payments from the manufacturers of vaccines</p> <p>A study funded by Okairos, initiated prior to his appointment to JCVI, was completed during 2016</p> <p>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.</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 from Gilead, MSD, GSK and Astra Zeneca.</p>
Prof Anthony Harnden (Deputy Chair)
<p>Professor Harnden has no registered conflicts of interest.</p>
Dr Andrew Riordan (Deputy Chair)
<p>Dr Riordan has no registered conflicts of interest.</p>
Prof Judith Breuer
<p>Professor Breuer has no registered conflicts of interest</p>
Dr Peter Elton
<p>Dr Peter Elton has no registered conflicts of interest</p>
Prof Adam Finn
<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>
Prof Matt Keeling
<p>Professor Matt Keeling has no registered conflicts of interest.</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

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 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
Dr Lucy Jessop (co-opted member)
Dr Lucy Jessop has no registered conflicts of interest

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Dr Lorna Willocks (co-opted member)
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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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DRAFT

Summary of Stakeholder Response

Responses

Responses were received from the Alliance for Natural Health (ANH), Anal Cancer Foundation (ACF), The Association for Cancer Surgery (BASO), British Association for Sexual Health and HIV (BASHH) British Medical Association (BMA), British Dental Association (BDA), Cancer Research UK (CRUK), Faculty of Sexual and Reproductive Healthcare (FSRH), GlaxoSmithKline (GSK), HPV Action, men and boys coalition, Merck Sharp & Dohme Ltd (MSD), National association of laryngectomee clubs, Oral Health Foundation (OHF), Royal College of General Practitioners (RCGP), The Sexual Health Charity (FPA), Stonewall, Terrence Higgins Trust (THT), Time for Action (TA).

A number of personal emails were also received from individuals including Prof Giampiero Favato (who advises HPV Action) and Dr David Conway (who is an invited expert to the HPV Subcommittee).

Most of the responses were pro vaccination of adolescent boys and disappointed with the JCVI interim advice not recommend a programme including boys. HPV Action represents a lot of the stakeholders and provided a comprehensive response regarding the interim decision. Many of the stakeholders followed the themes highlighted by HPV Action. Some of the responses (ANH,TA) , including personal emails, were against extending HPV vaccination to boys.

The main themes highlighted by the stakeholder response are outlined below:

Process

- The work used to inform the decision was not made publically available and so limited the opportunity for stakeholders to scrutinize this.
- Additional time for the stakeholders to respond was requested in the event of full disclosure of the modelling work.
- The JCVI had made its decision despite the fact that the PHE work has not been peer reviewed
- The Committee should also consider the cost effectiveness of a boys only programme

Modelling work

Costs

- Indirect costs should be taken into account and the full range of costs used should be made available. The very high costs of treatment rehabilitation and palliation for head and neck cancers should be included.

Epidemiology

- The attributable fraction for oropharyngeal cancer used is much lower than the CDC estimate of 60% and the continued trend of the increased incidence in these cancers should also be accounted for. Sensitivity analyses could test

the cost effectiveness of an upper limit of the aetiological fraction which is closer to that of the CDC estimate.

- The attributable fraction for anal cancer is also too low
- The modelling work should also account for nasal and paranasal sinuses and recurrent respiratory papillomatosis

Sexual behaviour

- Sex with unvaccinated women (abroad and in the UK) and older women and older men should be taken into account
- The Natsal 3 survey is already out of date and sexual behaviour is changing rapidly due to apps such as 'Tinder'
- A programme for boys would help to relieve the pressure on sexual health services

Herd effects

- All the modelling work considered overestimates the herd effects of the programme

MSM

- The targeted programme for MSM is too little too late, not enough, and not the best strategy (which is to vaccinate adolescent boys) as MSM are already exposed to HPV by the time they visit sexual health services and not all MSM will receive the vaccine or self-declare their sexuality.
- The targeted programme for MSM should not be taken into account as part of the consideration of extending vaccination to boys and should only be considered as a catch up programme in the event of a boys programme going ahead.
- JCVI should wait for the outcome of the MSM pilot before making any decision about boys
- The targeted programme for MSM discriminates against heterosexual males and forces disclosure of sexuality

Vaccine confidence

- The consequences of a fall in uptake should be taken into account and a boys programme should be introduced to pre-empt any potential drop. Sensitivity analysis should be included which looks at CE of boys programme with a lower uptake in girls.

Equality

- JCVI has not taken due regard on equality and should take full and proper account of this issue
- Women aged 18-45 are also denied access to the vaccine
- There is no screening protocol for anal cancer
- JCVI should request a new equality impact assessment
- Girls and women should not have the burden of providing protection for the whole population against HPV
- This issue will be raised with the equality and human rights coalition
- Cultural considerations should be taken into account when considering who should get the vaccine

- Findings from a KPA study suggest that once informed about the nature of HPV and its impact on male sexual health, the vast majority of parents would favor vaccination of their sons. Issues around health equity both in terms of responsibility for sexual health and protection against cancer were important to parents.

Manufacturers

GSK [the manufacture requested that their response remain confidential].

MSD gave a similar response along the lines of those raised by HPV Action above but also suggested changing the terms of reference of the HPV programme from its primary objective of reducing the incidence of cervical cancer.

Correspondence against including boys

- On grounds of vaccine safety, questioning the evidence on effectiveness, and in support of sex education and lifestyle changes.
- The safety concerns on girls should be resolved first and then only males at high risk should be targeted.

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