This minute will remain draft until ratified by JCVI at its next meeting.

JOINT COMMITTEE ON VACCINATION AND IMMUNISATION

Minute of the meeting held on Wednesday 2 February 2011
10.30am – 4.00pm
Skipton House, 80 London Road
London, SE1 6NX

Members

Professor Andrew Hall (Chair)
Dr Syed Ahmed
Dr Peter Baxter
Professor Ray Borrow
Professor Judith Breuer
Professor Alan Emond
Professor Jonathan Friedland
Dr Anthony Harnden
Dr Jennifer Harries
Mr Daniel Jackson
Professor Matt Keeling
Dr Gabrielle Laing
Mrs Pauline MacDonald
Mrs Anne McGowan
Dr Andrew Riordan
Dr Richard Roberts

Invited observers and presenters

Dr Stephen Inglis (NIBSC)
Dr Mary Ramsay (HPA)
Ms Joanne White (HPA)
Professor Elizabeth Miller OBE (HPA)
Dr Claire Cameron (Health Protection Scotland)
Prof John Watson (HPA)
Dr David Hill (NaTHNaC)
Lt Col Peter Hennessey (MoD)
Dr Linda Diggle (Jersey Health Dept.)
Dr Darina O'Flanagan (Eire)
Dr Phil Bryan (MHRA)
Professor John Edmunds (LSHTM / HPA)
Dr Mark Baguelin (HPA)

Devolved administrations

Dr Andrew Riley (Scottish Government)
Dr Elizabeth Reaney (DHSSPSNI)
Dr Sara Hayes (Welsh Assembly)

DH

Professor David Salisbury CB
Dr Dorian Kennedy
Dr Tom Barlow
Dr Stephen Robinson (minute)
Dr Keith Perry (minute)
Dr Tom Fowler
Mrs Lisa Vallente-Osborne
Mr John Henderson
Dr Peter Grove
Mr Guy Walker
Ms Clare Hensman
Mr David Jordan

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I. Welcome and announcements

1. The Chair welcomed all to the meeting. Apologies had been received from Professor Claire-Anne Siegrist and Dr Patricia Moore. The committee was reminded that some of the papers had been provided in confidence and that the papers should not be circulated or the information they contain discussed outside of the meeting.

II. Minutes of previous meetings

2. The committee agreed that the minute of the meeting for 6 October 2010 was an accurate record with the following changes:
    - Paragraph 9, line 3 – change 'boosting should remain' to 'boosting should not remain'.

3. The committee agreed that the minute of the teleconference on 30 December 2010 was an accurate record with the following changes:
    - Paragraph 5 – change 'in younger ages' to 'people aged under 65 years'.

III. Matters arising

4. The action points recorded in the 6 October 2010 meeting minute were reviewed. The Chair noted that:
    - JCVI and its travel sub-committee had commented on the draft rabies chapter of the Green Book and the chapter had been redrafted to address the comments received. Once issues around the implementation of some aspects of the advice have been resolved, the chapter would be circulated to members for final comment;
    - JCVI had commented on guidance on the use of multi-dose vials for the Green Book and the section had been drafted to incorporate the comments received and would now be included in chapter four of the Green Book;
    - he had written to the Chair of the ACDP regarding the committee's advice on influenza vaccination of poultry workers. ACDP had accepted JCVI's advice;
    - the DH Health Protection Analytical Team had completed the revised analysis of priority groups for pre-pandemic influenza vaccination and this would be considered under agenda item seven;
    - a response had been provided to the consultation of the Chief Scientific Advisor's draft Code of Practice of Scientific Advisory Committees; and
    - a paper on the use of polio vaccines for outbreaks had been provided that would be considered under agenda item nine.

5. At the last JCVI meeting, the committee considered a cost effectiveness analysis of seasonal influenza vaccination of pregnant women produced by the HPA. Members had noted there was uncertainty about estimates of some of the economic parameters used. Further discussions with the HPA modelling group following the meeting had confirmed that these uncertainties had been handled appropriately in the modelling study.

6. The committee was informed that the precise timing of the reconstitution of JCVI is not yet clear but it would happen prior to 1 April 2012.

7. The chair noted that there had been insufficient resources to plan and organise an open meeting of JCVI. Nevertheless, the committee was committed to the idea and an open meeting in the future remains a possibility depending on secretariat resources and the need to progress other JCVI-related work.

8. It was noted that the annual horizon scanning exercise would be undertaken during March and April in a similar manner to that conducted last year. The proposed scope of the horizon scan was discussed and in addition to information from vaccine developers on vaccines in the pipeline, the scope would include specific requests for information on new pneumococcal vaccines and a call for evidence on new seasonal influenza vaccines, as proposed by the JCVI pneumococcal and influenza sub-committees, respectively. The committee also asked the secretariat to include a request for information on vaccine manufacturer's plans to produce for the UK market egg protein-free seasonal influenza vaccines for use in both adults and children from 6 months of age.

IV. Coverage of childhood vaccines and draft Hepatitis B guidance

Coverage

9. The committee considered childhood vaccine coverage data for England, Scotland, Wales and Northern Ireland for the quarter July-September 2010.

10. In England, reported coverage was similar to that of the previous quarter at 93 per cent for the primary immunisations (DTaP/IPV/Hib, PCV2 and MenC) by 12 months of age. DTaP/IPV/Hib had risen to 95 per cent with MMR1 at 88.3 per cent at 24 months of age. Data on coverage from the MMR sentinel surveillance scheme suggested a continued increase in coverage for England should be expected in the coming months. Hepatitis B coverage was 78 per cent by 12 months of age for children who were born to hepatitis B surface antigen positive mothers, a slight decrease on that seen the previous quarter.
http://www.hpa.org.uk/hpr/archives/2010/hpr5010.pdf

11. The committee noted the very low coverage recorded by Haringey Teaching PCT and asked DH to raise that issue with the appropriate body.

ACTION: Secretariat to contact London Strategic Health Authority to enquire about the reasons for the low coverage recorded by Haringey Teaching PCT and the actions that were being undertaken.

12. In Scotland, reported coverage was 97 per cent for primary immunisations (DTaP/IPV/Hib) at 12 months of age and MMR1 at five years of age was over 96 per cent.

http://www.isdscotland.org/isd/servlet/FileBuffer?namedFile=child_imms_LatestRates_Quarter310.xls&pContentDispositionType=attachment

13. In Wales, reported coverage was similar to the last quarter with 16 of the 22 local authority areas reporting coverage of over 95 per cent. MMR1 and Hib/MenC coverage had decreased from the previous quarter with 95.4 per cent of children receiving two doses of PCV by 12 months of age and 91.3 per cent for MMR1 by 24 months of age.
http://www2.nphs.wales.nhs.uk:8080/VaccinationsImmunisationProgsDocs.nsf/3dc04669c9e1eaa880257062003b246b/3e538c1741ff083d802577dc00500080/$FILE/Cov10q3%20(report96).pdf

14. In Northern Ireland, reported vaccine coverage of all primary immunisations at 12 months of age was over 97 per cent. At 24 months of age, coverage of DTaP/IPV/Hib was 98.7 per cent. By five years of age, MMR coverage is 96.7 per cent and MMR2 at 91.1 per cent.
http://www.cdscni.org.uk/surveillance/Coveragestats/default.asp

Hepatitis B guidance

15. The committee was presented with draft 'best practice' guidance for Hepatitis B antenatal screening and newborn immunisation prepared by the Department of Health (DH). The committee had raised concerns in previous meetings about the low coverage and completion rates of hepatitis B vaccination in children born to hepatitis B surface antigen positive mothers. The 'best practice' guidance was aimed at both commissioners and providers and had been developed so that it could be used now and following the planned structural changes within the NHS. The purpose of the document was to set out the roles and responsibilities of heathcare professionals with the aim of achieving better information flow between those who give the initial and those who give subsequent doses of hepatitis B vaccine to improve coverage and completion rates for this immunisation.

16. The committee welcomed and commended the development of this important guidance. The committee was generally content with the guidance but made a number of suggestions for minor changes or additional aspects to consider:
    - the use of the term 'Guthrie test' should be used with care as it is linked specifically to neonatal screening;
    - the use of the term 'immunisation coordinator' may be misleading as the role might depend on the organisational setting. An alternative descriptor should be considered that accurately describes the role and responsibilities;
    - it is important that the guidance makes clear that one person should be identified as having overall responsibility for the commissioning, and one person should be identified as having responsibility for ensuring the provision, of the service;

- given that high viral load is an indication for use of immunoglobulin, it was noted that testing of the mother for viral load might be considered to determine if immunoglobulin should be administered to the infant;
- PCHR definitions are incorrect and should be revised;
- specific guidance around universal notification systems to automate the notification of Hepatitis B status should be considered; and
- it may help notifications if laboratories were given more responsibility to proactively inform clinicians about the need for neonatal hepatitis B vaccinations should laboratory results from testing of the mother the indicate that the infant is at risk of hepatitis B.

17. The committee indicated it would be content to review a further iteration of the guidance by correspondence.

ACTION: DH to circulate changes to the committee for final comment

V. Report of the JCVI influenza sub-committee

18. The sub-committee Chair referred to the minute of the influenza sub-committee meeting and explained that the sub-committee had considered:
    - preliminary modelling study to address recommendation 22 in the Hine review of the 2009 influenza pandemic. This recommendation had suggested a study be conducted to inform future decisions about the level of coverage of pandemic-specific vaccine needed to substantially reduce morbidity and mortality in the event of an influenza pandemic. This work was on going and the sub-committee had provided advice on the direction of the work. A completed analysis addressing the sub-committee comments would be presented to JCVI at its June 2011 meeting.
    - an update to a modelling study considered by JCVI at its October 2010 meeting on the priority groups to receive pre-pandemic flu vaccine. This study would be considered under agenda item seven.
    - an ongoing modelling study to assess the impact and cost effectiveness of the seasonal influenza vaccination programme and possible extensions to the programme that would be considered under agenda item six.
    - a preliminary paper on new types of seasonal influenza vaccines. This work would continue and be informed by a call for evidence on seasonal influenza vaccines in parallel with the horizon scanning planned for March and April 2011. It had been noted that data from head to head clinical trials of influenza vaccines to allow the performance of vaccines to be compared are often lacking.
    - a number of recently published studies noting that:
        - uptake of seasonal influenza vaccine by frontline healthcare workers during the 2009/10 winter was disappointing.
        - no evidence of an association between the use of seasonal influenza vaccines and febrile convulsions in children in the UK had been found.
        - a study of paediatric mortality had found different relative risks to H1N1v

associated with clinical risk factors and, whilst the study had found an increased risk with ethnic background, this finding was based on a small number of subjects and may not be generalisable.
- there had been no evidence for significant antigenic change in the H1N1v virus in the UK.
- a small study had shown influenza vaccine to be effective in young children in contrast to previous data.

19. The committee accepted the advice from the sub-committee.

20. The committee was informed that surveillance by the Medicines and Healthcare products Regulatory Agency continued to find no observed excess of febrile convulsions from the use of influenza vaccines in the UK during the course of the 2010/11 influenza season.

21. The committee agreed that uptake of seasonal influenza vaccine by frontline healthcare workers needed to improve further. The committee suggested that work could be done with the medical professional bodies and noted that DH had begun working on improving influenza vaccination with the Social Partnership Forum, that included the professional bodies and Unison. As there is wide variation in uptake between Trusts, it was suggested that the approaches followed by Trusts where uptake is high should be studied for possible wider dissemination. A study of approaches used to vaccinate frontline healthcare workers during the pandemic also provided indications of effective approaches.

22. The committee noted that there is some evidence that frontline healthcare workers may not consider influenza vaccination to be effective in preventing influenza and that this view may have may have stemmed in part from the findings of a Cochrane review of influenza vaccination of healthcare workers[1]. The committee considered this review to be based on a highly flawed interpretation of the evidence and did not support the findings of the report.

VI. Influenza and revisions to the influenza Green Book chapter

Review of 2010/11 influenza season

23. The committee was provided with latest data on the epidemiology of the 2010/11 influenza season by HPA. Influenza activity had risen through December 2010, peaking around end December / early January followed by a decline in activity through January. H1N1v had been the dominant influenza strain. The UK had been amongst the first countries in Europe to experience increased influenza activity which had moved eastwards subsequently across Europe. In contrast, the H3N2 strain had been dominant during the North American 2010/11 influenza season.

[1] Thomas RE, Jefferson T, Lasserson TJ. Influenza vaccination for healthcare workers who work with the elderly. Cochrane Database of Systematic Reviews 2010, Issue 2. Art. No.: CD005187. DOI: 10.1002/14651858.CD005187

24. The committee was provided with preliminary unpublished mid-season estimates of the effectiveness of trivalent seasonal influenza vaccine given during the 2010/11 season and also when monovalent H1N1v vaccine had been given during the 2009 pandemic. The committee noted the wide confidence intervals around the estimates. The data suggested a rank order of protection: trivalent seasonal influenza vaccine and monovalent H1N1v vaccine, followed by trivalent seasonal influenza vaccine only, followed by monovalent H1N1v vaccine only. These data suggest that immunity from one dose of adjuvanted monovalent H1N1v vaccine given during the 2009 pandemic had waned appreciably over the course of 2010. The committee noted that, whilst data from the study provided estimates of vaccine effectiveness against infection, they gave no indication on the effectiveness of the vaccine against severity of disease. This would be important to establish. It was noted that data from Flusurvey, a web-based monitoring system, had shown a similar trend in vaccine effectiveness against infection and had also suggested that vaccination was effective at least against mild illness. It was possible that the Fluwatch study might also provide data on the effectiveness of vaccination against severity of disease.

25. The committee asked about the collection of data on fatal cases of verified influenza infection. HPA explained that these data had been collected during the 2009 pandemic and had provided information on the characteristics of cases – the presence and type of clinical risk factors, age and vaccination status. It was important to recognise that under ascertainment of fatal cases is highly likely particularly in the elderly as fewer deaths may be extensively investigated in that age group. There may also be regional variation in ascertainment and a variable lag time in identifying suspect cases and then verifying the involvement of influenza. It was possible that early conclusions drawn from a small data set may be misleading: for example, early data from the 2010/11 influenza season suggested a slightly higher risk of mortality in children than was apparent later with a larger dataset. This type of surveillance had been amongst the earliest indicators of the re-emergence of H1N1v activity during the 2010/11 winter. Work is planned to improve the ascertainment of influenza verified deaths and to look at harmonising the surveillance of influenza verified deaths as well as other influenza surveillance systems across the UK, as had been recommended by the Hine Review of the 2009 pandemic.

26. The committee noted that analysis of the characteristics of fatal cases of verified influenza infection from the 2010/11 influenza season suggested that few had received trivalent seasonal or pandemic influenza vaccine and around three quarters were in individuals from the defined clinical seasonal influenza risk groups. Relative risk analysis of clinical risk groups showed that those in the clinical risk groups combined were around 20 times more at risk of death from influenza than those with no underlying health conditions. Similar analysis by age groups suggested that those aged 45-64 years followed by those aged 65 years of older were most at risk of death from influenza. Immunosuppression, neurological

disease and respiratory disease including asthma were the most represented clinical risk factors. Overall the deaths in those with clinical risk factors were of a similar distribution to that seen during the 2009 pandemic, although older age groups may have been more affected during 2010/11 influenza season than during the pandemic. Noting that many of the deaths in those with neurological disease were young adults and children with neuro-developmental problems, the committee asked if a sub-analysis could be conducted to assess the relative risk of more specific conditions, in particular different neurological conditions.

ACTION: The HPA to assess the feasibility of a sub-analysis to assess the relative risk of more specific condition and conduct such an analysis, if feasible.

27. The committee noted that many more 'all cause excess deaths' had been observed from Office of National Statistics data during the 2010/11 influenza season than during the 2009 pandemic. As cause of death cannot be established from these data, the deaths could not be attributed to influenza directly. There may be a wide range of causes including the very cold 2010/11 winter, other infections and co-infections. Increased virological and microbiological testing as part of hospital-based surveillance would be very valuable in allowing better determinations of the causes and their contribution to severe illness, particularly during the winter when there may be numerous and multiple possible causes.

    ACTION: The HPA to assess the feasibility of hospital surveillance combined with virological and microbiological testing to allow better determinations of the causes and their contribution to severe illness.

28. The committee noted that, whilst the re-emergence of the H1N1v virus during the 2010/11 winter had been predicted, the extent of H1N1v activity had been much larger than expected. Potential explanations included more rapidly waning immunity following first infection than had been originally thought. Whilst much of the older population seemed to have long-term immunity to H1N1v acquired from exposure to an H1N1 virus during and following the 1957 influenza pandemic, it is possible that repeated exposure to the same or a similar virus may be required to develop such long-lasting immunity. Alternatively, it is possible that a hitherto undetected functional mutation of the H1N1v virus had arisen that had altered population susceptibility to, and/or the transmissibility of, the virus. Environmental conditions such as temperature may also have played a role i.e. the colder weather during the 2010/11 winter compared with the 2009 autumn. The committee agreed that further serological studies are needed to understand the possible change in population immunity to H1N1v during 2010. It was noted that the Fluwatch study may provide data on the waning of protection following infection and the proportion of re-infections.

29. The committee agreed that a review should be conducted on the data needed for, and limitations of, modelling studies of influenza epidemics to better understand the

uncertainties in such modelling. The Chair indicated he would write to the Chair of the Scientific Pandemic Influenza Advisory Committee (SPI) about such a review.

ACTION: Chair to discuss a review of pandemic influenza modelling with the SPI Chair.

30. The committee considered data from the weekly monitoring of seasonal influenza vaccine uptake in England during the 2010/11 influenza vaccination programme. It was noted that vaccine uptake had slowed slightly during October/November compared with previous seasons. Anecdotal evidence suggested that the uptake rate may have been adversely affected early in the vaccination programme by unfounded concerns about the safety of the H1N1v component of the seasonal influenza vaccine. However, later in the programme, concern about severe illness caused by H1N1v influenza may have increased the uptake rate. Whilst uptake in the group aged 65 years and older had now exceed 70% for a number of years, there is a clear need to increase uptake in clinical risk groups aged below 65 years.

31. The committee noted that data from Scandinavian countries had suggested a possible association between Pandemrix® vaccination and a small increased risk of narcolepsy; however a causal link had not been established and further investigations are underway. Studies in other countries including the UK had failed to find any such association.

Cost effectiveness modelling

32. The HPA summarised progress on the proposed epidemiological and economic modelling of the seasonal influenza programme that had been agreed with JCVI in 2010. Initially it had been proposed that two approaches would be taken: a regression analysis and a transmission dynamic analysis. However, data were insufficient particularly on the population immunity either from natural exposure or vaccination before, during and after influenza seasons to allow the regression analysis to be progressed. Instead, only a transmission dynamic modelling approach was being followed. A preliminary analysis had been conducted using data from the 2006/7 influenza season – a season not especially mild nor severe in nature and where one influenza A strain had circulated. A number of scenarios had been examined in which the effectiveness of the vaccine and the severity of the influenza season, in terms of GP consultations, hospitalisations and deaths, had been varied. This analysis suggested that the vaccination of those aged 65 years and older and those under 65 years in clinical risk groups is likely to be cost effective except in circumstances where a vaccine was poorly matched to circulating influenza strains in a mild influenza season. It was noted that in recent years, with the exception of the 2009 pandemic, seasonal influenza vaccines had been well matched to the circulating influenza strains.

33. The committee considered it important that serological studies were supported to understand better the development and duration of population immunity to influenza and to support epidemiological and modelling studies.

34. The committee noted that the preliminary cost effectiveness study of the seasonal influenza vaccination programme was based around a single influenza season with a single influenza strain in circulation. However, whilst it is rare that two influenza A strains circulate together, influenza B is often present with an influenza A strain. There is also considerable variability in the severity of disease and extent of influenza activity from one season to the next. It was noted that, whilst the age distribution of influenza illness was skewed to older ages in influenza seasons prior to the 2009 pandemic, a greater proportion of younger age groups were affected by the H1N1v strain. This differing age distribution may continue to be observed in future influenza seasons if this strain predominates. Thus, modelling of influenza outbreaks fitted to data collected prior to the pandemic may not be closely representative of outbreaks occurring in years following the pandemic in terms of the age distribution of infections and illness. It was noted that modelling the cost effectiveness of vaccinating individual clinical risk groups would be difficult because of limitations in the data available.

35. The committee agreed that, despite the limitations, it was reasonable to use the 2006/7 season as an initial basis for the model and to look at other pre-pandemic influenza seasons to develop the model as data are available. Both the effect of vaccination on transmission and severity of disease should be considered. The study should look at the incremental cost effectiveness of extending vaccination to the following age groups both individually and combined: 6 months to below five years, five years to below 17 years, 50 years to below 65 years and the entire population. The study should consider the need for two doses to be given to children under 13 years that had not previously received seasonal influenza vaccine. It should also be borne in mind that some seasonal influenza vaccines are not licensed for use in some age groups and that different types of seasonal influenza vaccines may be available in the future that may be indicated or contraindicated for certain age groups and the costs of different types of seasonal influenza vaccines may vary.

36. The committee agreed that, based on the evidence available, it would not advise changes to the groups of patients targeted for influenza vaccination in the 2011/12 influenza season. Thus, the following patient groups should be offered seasonal influenza vaccine in the 2011/12 programme: all those aged 65 years and older, those aged six months to below 65 years in the seasonal influenza clinical risk groups including pregnant women. Potential widening of the seasonal influenza vaccination programme to include other healthy age groups of the population would be considered based on the findings of the completed cost effectiveness study being conducted by HPA. HPA agreed that the study would be completed over the next few months in time for the study to be peer-reviewed jointly by the JCVI influenza sub-committee, health economists and the SPI modelling subgroup. The final study

would be considered at the October 2011 JCVI meeting and would inform the committee's advice about the groups that should be offered seasonal influenza vaccine in the 2012/13 influenza season.

ACTION: The HPA to complete the study for peer-review. Secretariat to convene a joint meeting of the JCVI influenza sub-committee supplemented by health economists and SPI modelling subgroup to allow a final study to be considered at the October 2011 JCVI meeting.

37. The committee welcomed a suggestion by the Chair that in future all mathematical modelling studies should be accompanied by a summary of the key assumptions, data inputs and parameter estimates together with the sources of each.

Influenza Green Book chapter

38. The committee reviewed a draft influenza Green Book chapter in preparation for the 2011/12 influenza vaccination programme. The committee agreed that:
    - all pregnant women should be offered seasonal influenza vaccine irrespective of trimester of pregnancy as they are at risk from influenza during all stages of pregnancy and are to be considered to be in a clinical risk group for seasonal influenza vaccination.
    - whilst evidence suggests that women may continue to be at increased risk of influenza for several weeks post-partum, given the time needed for an immune response to develop following vaccination, seasonal influenza vaccination would provide little protection during the period of increased risk. Therefore, the offer of seasonal influenza vaccination should not be extended to women post partum. Seasonal influenza vaccine during pregnancy would provide protection for mothers and their newborn.
    - 'severe neurological disability' should be added to the examples listed under chronic neurological disease in the table of clinical risk categories as this was risk factor for influenza.
    - since the summary of product characteristics for seasonal influenza vaccines are currently unclear about the dose of vaccine for young children, the Green Book should indicate that a full dose of vaccine should be administered to children from six months of age as there is evidence from a recent study that this dose is effective in young children[2].
    - in the absence of egg protein-free seasonal influenza vaccines, seasonal influenza vaccines with the lowest egg protein content should be used for those with egg allergy with vaccination of those with severe (anaphylactic) egg allergy undertaken by a specialist in hospital using a split-dose protocol.

39. A number of editorial amendments were proposed. In addition, it was suggested that a search should be undertaken for recent studies on the immunogenicity or

[2] Heinonen S, Silvennoinen H, Lehtinen P, Vainionpää R, Ziegler T, Heikkinen T (2010) Effectiveness of inactivated influenza vaccine in children aged 9 months to 3 years: an observational cohort study. *Lancet Infect Dis.* 2010 Nov 22. [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/21106443

effectiveness of one versus two doses of vaccine in children that have not previously received seasonal influenza vaccine and these studies included.

40. The committee considered correspondence received by the Chair about the specific inclusion of those with epilepsy or Myalgic Encephalopathy (ME) in the seasonal influenza clinical risk groups for vaccination. The committee noted that there is heterogeneity in these conditions. Most individuals with epilepsy are well controlled and have no co-morbidity and therefore influenza is not different for them compared with the healthy population. Individuals with severe neurological disability are at greater risk from influenza and may also have epilepsy and would warrant vaccination but for reason of their neurological disability not epilepsy. ME is a poorly defined syndrome with a number of different phenotypes in children and adults. As it is unclear that seasonal influenza vaccination is warranted in all of these phenotypes, the committee advised that whether or not those with ME are vaccinated against influenza should be an individual clinical decision based on a patient's medical history. The committee agreed that neither epilepsy nor ME should be included in the influenza Green Book chapter as specific indications for seasonal influenza vaccination.

ACTION: Secretariat to revise influenza Green Book chapter as indicated.

VII. Target groups for pre-pandemic influenza vaccine

41. The committee considered advice from its influenza sub-committee and findings from modelling studies on the use of a pre-pandemic influenza A H5N1 vaccine from a stockpile of about 8 million courses (16 million doses). This advice and modelling assessed the impact on severity and transmission of pandemic influenza of vaccination of various groups of the population. The committee acknowledged that the high degree of uncertainty about the nature of the pandemic virus and the effectiveness of the vaccine makes assessment of the potential impact of pre-pandemic vaccination strategies difficult and concluded that:
    - those in the seasonal influenza clinical risk groups should be prioritised to receive the vaccine. This is because there is greater benefit from vaccinating clinical risk groups in order to lower morbidity and mortality under many scenarios (i.e. those where the relative risk of the pandemic influenza to clinical risk groups is more than five-fold greater compared with healthy groups). Furthermore, whilst targeting children in order to potentially lower transmission may be more beneficial under some scenarios, the added benefit of targeting vaccination to children compared with clinical risk groups appeared small. In addition, there is greater uncertainty about the impact of this approach than about the impact of pre-pandemic vaccination of risk groups.
    - the benefit of pre-pandemic vaccination on the effectiveness of pandemic-specific vaccine may be small if the pandemic-specific vaccine only became available late in a pandemic. Thus, it would be important to maximise the benefit of a pre-pandemic vaccination programme.

- a single dose vaccination strategy would allow twice as many people to be vaccinated and could allow many more people to be vaccinated before the pandemic virus becomes widespread as patients would not need to be recalled for a second dose. If more than half of the protection derived from two doses of vaccine is achieved following administration of a first dose then a greater benefit overall would be realised from single doses compared with a two dose vaccination strategy. Whilst immunity may wane to a greater extent with a single compared with a two dose strategy, waning following pre-pandemic vaccination may not be appreciable over the course of the first (if there is more than one) pandemic wave. It would be important to assess the immunological response from one dose versus two doses of the pre-pandemic vaccine, which may differ between age and clinical risk groups of the population.

VIII. Report from the JCVI pneumococcal sub-committee

42. The committee was provided with a presentation by the HPA on the impact of the childhood pneumococcal vaccination programme and of the routine adult vaccination programme for those aged 65 years and older along with data on the effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPV23). The sub-committee Chair referred to the minute of the pneumococcal sub-committee meeting and summarised the advice from the sub-committee.

43. Following consideration of the epidemiological data on the impact of vaccination programmes on pneumococcal disease and the sub-committee's advice, the committee strongly advised against use of the PCV10 vaccine when PCV13 was available as epidemiological evidence suggested that the use of a vaccine that offered less protection against pneumococcal disease would appreciably undermine the direct protection against pneumococcal disease provided to children, and the indirect protection against pneumococcal disease provided to older adults.

44. The committee noted that epidemiological evidence suggested that there had been no discernable decrease in the incidence of pneumococcal disease in those aged 65 years and older from the routine adult pneumococcal vaccination programme using PPV23. Instead a significant decrease in pneumococcal disease in that age group had been observed following the introduction of seven valent pneumococcal conjugate vaccine (PCV7) into the childhood vaccination programme, especially in disease arising from the seven pneumococcal serotypes that the conjugate vaccine provided protection against. Whilst this had been tempered by increases in disease from other pneumococcal serotypes, indications suggest that following the recent replacement of PCV7 with PCV13, a further decline in disease from the additional six serotypes can be expected.

45. The committee noted that epidemiological evidence suggested that the effectiveness of PPV23 in older adults is poor and of short duration. Given the poor effectiveness and duration of PPV23 in older adults and the lack of a demonstrable impact of the routine pneumococcal vaccination programme for those aged 65 years

and over, the committee agreed with the advice from the sub-committee and advised that this programme should be discontinued.

46. The committee noted that there is no evidence available yet that substituting PPV23 with PCV13 would provide protection that is more effective for older adults. However, this could be reviewed if data become available that show that this vaccine is effective in older adults.

    ACTION: The committee to issue a statement on the its advice in discontinuing the routine adult pneumococcal vaccination programme for those aged 65 years and older.

47. The committee noted that the sub-committee had advised that the current pneumococcal risk groups are broadly consistent with new data but that further data are being sought to establish the increased risk of pneumococcal disease for diabetics, patients undergoing invasive surgery, and patients at different stages of chronic kidney disease. In reviewing the sub-committee's advice on the pneumococcal vaccination of patients with an allogenic or autologous bone marrow transplant, the committee advised that these should be considered as a single group as the evidence that they should be treated differently was weak and both groups include patients with serious illness. The committee accepted the sub-committee's advice that there is a strong association between welding and pneumococcal disease and that the welders should be offered PPV23 vaccine through their employers.

48. The committee considered the sub-committee's advice about the wider use of PCV13 in clinical risk groups. It was noted that implementation of the advice would be extremely costly and currently data are limited on the relative risk of pneumococcal disease in clinical risk groups and on the relative benefit of one or two doses of PCV13. The committee asked that further analysis be undertaken to assess the relative risks of pneumococcal disease in clinical risk groups combined with an analysis of clinical trials data on the use of PCV vaccines in the different risk groups: for example those with asplenia had shown good responses to one dose of PCV and therefore the two-dose schedule may be unnecessary for this group. The committee would consider the wider use of PCV13 in clinical risk groups once this analysis had been completed. In the meantime existing Green Book advice should be followed. It was noted that PCV13 was currently not licensed for use in adults.

    ACTION: The HPA to conduct a study on the relative risks of pneumococcal disease in clinical risk groups and secretariat to prepare a paper using data from the HPA study and data from clinical trials to inform further JCVI considerations.

49. The committee accepted the advice from the sub-committee that mass pneumococcal vaccination using PPV23 as a countermeasure against pandemic influenza would not be cost effective and is not advised.

IX. Vaccines for polio outbreaks

50. The committee considered a paper presenting options for the control for polio outbreaks with polio vaccines.

51. The committee noted that the standard intervention in countries that have recently had polio outbreaks was with World Health Organization (WHO) pre-qualified oral polio vaccines (OPV), monovalent type I or type III (mOPV) or bivalent (bOPV) type I and III. The UK could have access to large numbers of doses of outbreak strain specific vaccine if prior arrangements are put in place. While these vaccines would not be licensed for use in the UK, they would be WHO pre-qualified and manufacture batch tested but not necessarily tested by a UK official medicines control laboratory.

52. The committee noted that use of trivalent OPV (tOPV) in an outbreak carries a risk of re-introduction of additional strains of poliovirus and thus, any use of OPV should be restricted to the monovalent type causing the outbreak. As there is a lack of evidence on the use of IPV in outbreaks and there may be increased adverse reactions from widespread additional use of Td/IPV, the committee advised that mOPV is preferred to IPV in an outbreak.

53. JCVI advised that planning for any potential polio outbreak should ensure rapid access to stocks of mOPV and DH could consider the use of IPV containing vaccines such as Td/IPV as a contingency measure for immediate local implementation and until larger stocks of mOPV became available should they be needed. This might require some initial stockpiling of Td/IPV although such stocks could be rotated into routine use with a reserve for contingency use as a first response to a polio outbreak.

X. Submission on Hib-containing vaccines

54. The committee reviewed information submitted by GSK on its Hib-containing vaccines. This submission was in response to the committee's request, following the horizon scanning in June 2010, for further data on these vaccines.

55. The committee reiterated its previous advice that equivalent protection should be demonstrated against diphtheria, tetanus, pertussis, polio and Hib if replacement of the current combination vaccine with an alternative vaccine is considered.

56. The committee considered data in support of a number of different variations in the routine childhood vaccination schedule and concluded that:
    - combination vaccines containing antigens to diphtheria, tetanus, pertussis, polio and Hib are affected by the use of CRM_{197}-containing vaccines that are given at the same time, and can result in a decrease in the level of Hib protection with increasing use of CRM_{197}. It is important that current levels of Hib protection are at least maintained;

- antibody persistence data up to 12 months post booster for Menitorix used in 2+1 schedules would be valuable;
- further consideration should be given to the use of combination vaccines that contain the hepatitis B antigen but only alongside other potential changes to the schedule.

ACTION: Secretariat to commission from HPA an analysis of different options for changes to the vaccination schedule to explore the possible introduction of a hepatitis B-contain vaccine.

XI. GRADE

57. The committee considered the application of the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system to the review of scientific information provided to JCVI. It was noted that the committee currently assesses a comprehensive body of evidence using papers and information from a wide range of sources. This had proved to be an effective system for compiling evidence for committee review, however, the evidence is not graded formally.

58. It was noted that application of GRADE includes the use of a common methodology to rate the quality of evidence and the strength of recommendations. The committee noted that other immunisation advisory groups were considering the adoption of GRADE. In the US, the Advisory Committee on Immunization Practices had recently agreed to adopt a modified version of GRADE.

59. The committee recognised that implementing the GRADE system would be resource intensive. Proposals to make international grading of publications accessible via the web might help to lessen the burden of work. The committee agreed that the evidence needs to be graded by individuals with an understanding of vaccine data, and that there may be different weightings applied depending on country-specific data. In addition, the strength of data may be viewed differently by different groups. While randomised controlled trials score higher in the GRADE system, observational studies and clinical expert advice are important aspects of forming vaccination policy advice.

60. The committee suggested that GRADE training be identified for JCVI members and the secretariat. A topic could be identified for trained individuals to test system.

ACTION: Secretariat to identify GRADE training providers.

XII. Papers for information and any other business

61. The committee discussed a review paper by Shoenfeld and Agmon-Levin (2010)[3] on autoimmune/inflammatory syndrome induced by adjuvants, in particular on the role of adjuvants in the pathogenesis of four conditions: siliconosis, the Gulf war syndrome (GWS), the macrophagic myofasciitis syndrome (MMF) and post-vaccination phenomena. The committee considered that the paper did not provide convincing data on the role of adjuvants in these four 'enigmatic' medical conditions and that the review did not raise safety concerns about the use of adjuvants.

62. A DH consultation on a value-based approach to the pricing of branded medicines was discussed. This proposes the introduction of a system of value-based pricing so that patients can access the medicines and treatments their clinicians consider would be beneficial. The system would apply different weightings to the benefits provided by new medicines for innovation, impact against burden of illness and societal benefits, which would imply a range of price thresholds reflecting the maximum price that someone was prepared to pay. The committee considered that the document is currently unclear in a number of areas, including whether the system will cover vaccines, about applying QALYs, or about who decides on value.

    ACTION: Secretariat to draft a response for the committee to the consultation.

63. The committee raised issues in connection with aspects of the public health white paper and associated consultation documents. Members identified a potential risk about the separation of funding and commissioning routes for immunisation services and the potential for loss of public health expertise and performance management at local level. For example, in relation to the commissioning of hepatitis B vaccination of at risk infants, the initial dose is administered within the Acute Trusts, but it is unclear who would be responsible for administering the necessary subsequent doses. In addition, there is little clarity currently about the expertise and management that would be available to deliver the adolescent vaccine programme within local authorities. The committee also suggested that there might be a perceived loss of independence of the expertise currently provided by the HPA once staff transfer to Public Health England. The committee rely heavily on a range of surveillance, research and other evidence that is currently provided independently by HPA. The committee suggested that the Chair write to the Secretary of State to highlight these concerns.

    ACTION: Chair to write to the Secretary of State for Health in response to proposals set out in the public health white paper and associated consultations.

XIII. Dates of future meetings

Wednesday 8 June 2011
Wednesday 5 October 2011
Wednesday 1 Feb 2012
Wednesday 13 June 2012

[3] Shoenfeld Y, Agmon-Levin N (2011) 'ASIA' - Autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun.* 36(1):4-8. http://www.ncbi.nlm.nih.gov/pubmed/20708902

This minute will remain draft until ratified by JCVI at its next meeting.

Wednesday 3 October 2012

The JCVI agenda and meeting papers are published on the meetings area of the JCVI website http://www.dh.gov.uk/ab/jcvi/index.htm

This minute will remain draft until ratified by JCVI at its next meeting.

Annex 1

Declarations of interest

Agenda Item VI and VII
The following members declared interests in companies that manufacture seasonal and pandemic influenza vaccines (Baxter, GSK, MASTA, Novartis, Pfizer, Sanofi-Pasteur MSD, Solvay):

Member	Interests	Action
Ray Borrow	Personal, non-specific Baxter, GSK, Novartis and Pfizer Non-personal, non-specific Sanofi-Pasteur MSD	The Chair ruled that the member was allowed to participate in the discussion and decision.
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member participated in the discussion and decision
Jon Friedland	Non-personal, non-specific Pfizer	The member participated in the discussion and decision
Pauline MacDonald	Personal, non-specific GSK Non-personal, non-specific Sanofi-Pasteur MSD	The Chair ruled that the member was allowed to participate in the discussion and decision.
Anne McGowan	Non-personal, non-specific GSK, Pfizer, Sanofi-Pasteur MSD	The member participated in the discussion and decision
Andrew Riordan	Personal, non-specific GSK	The Chair ruled that the member was allowed to participate in the discussion and decision.

This minute will remain draft until ratified by JCVI at its next meeting.

Agenda Item VIII
The following members declared interests in companies that manufacture pneumococcal vaccines (GSK, Pfizer and Sanofi-Pasteur MSD):

Member	Interests	Action
Ray Borrow	Personal-specific Pfizer Non-personal, specific Sanofi-Pasteur MSD and Pfizer	**The Chair asked the member to leave the room.**
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member participated in the discussion and decision
Jon Friedland	Non-personal, non-specific Pfizer	The member participated in the discussion and decision
Pauline MacDonald	Personal, non-specific GSK Non-personal, non-specific Sanofi-Pasteur MSD	The Chair ruled that the member was allowed to participate in the discussion and decision.
Anne McGowan	Non-personal, non-specific GSK, Pfizer, Sanofi-Pasteur MSD	The member participated in the discussion and decision
Andrew Riordan	Personal, non-specific GSK	The Chair ruled that the member was allowed to participate in the discussion and decision.

This minute will remain draft until ratified by JCVI at its next meeting.

Agenda Item IX
The following members declared interests in companies that manufacture polio-containing vaccines (GSK and Sanofi-Pasteur MSD):

Member	Interests	Action
Ray Borrow	Personal, non-specific GSK Non-personal, non-specific Sanofi-Pasteur MSD	The Chair ruled that the member was allowed to participate in the discussion and decision.
Judith Breuer	Non-personal, non-specific Sanofi-Pasteur MSD	The member participated in the discussion and decision
Pauline MacDonald	Personal, non-specific GSK Non-personal, non-specific Sanofi-Pasteur MSD	The Chair ruled that the member was allowed to participate in the discussion and decision.
Anne McGowan	Non-personal, non-specific GSK and Sanofi-Pasteur MSD	The member participated in the discussion and decision
Andrew Riordan	Personal, non-specific GSK	The Chair ruled that the member was allowed to participate in the discussion and decision.

This minute will remain draft until ratified by JCVI at its next meeting.

Annex 2

Evidence considered by the committee.

Agenda item 2:

- Minute of JCVI 6 October 2010 meeting
- Minute of JCVI 30 December 2010 teleconference

Agenda item 3:

- Note on 2011 horizon scanning
- New section for chapter 4 of the Green Book on use of multi-dose vials

Agenda item 4:

- COVER report: July to September 2010
- Coverage for England, Scotland, Wales and Northern Ireland
- Draft guidance on hepatitis B antenatal screening and newborn immunisation

Agenda item 5:

- Minute of the JCVI influenza sub-committee 1 December 2010

Agenda item 6:

- Draft Green Book chapter
- Proposal for the assessment of the impact of the influenza vaccination programme between 1995 and 2008 in the UK
- Publications relating to influenza vaccination of egg allergic individuals
- Commentary on the risk of narcolepsy observed among children and adolescents vaccinated with Pandemrix
- Publications relating to safety of influenza vaccination in pregnant and postpartum women
- Cumulative weekly uptake of influenza vaccine to 23 January 2011
- Draft publications on the effectiveness of seasonal 2010/11 and pandemic influenza vaccines in preventing influenza infection in the UK, and cost-effectiveness of the current seasonal influenza vaccination programme in England,
- Report on risk factors for death with influenza in the 2010/11 season

Agenda item 7:

- Note on target groups for pre-pandemic influenza vaccination
- Summary paper on modelling the use of 16 million doses of H5N1 pre-pandemic vaccine
- Paper on potential disadvantages and benefits of using a small stockpile of pre-pandemic vaccine as part of a 'prime and boost strategy' alongside pandemic-specific vaccine
- Paper on use of a targeted stockpile of pre-pandemic vaccine (considered by JCVI in Oct 2010) and an update from Nov 2010
- Paper from University of Warwick on pre-pandemic vaccination: what to do with the stock-pile

Agenda item 8:

- Minute of the JCVI pneumococcal sub-committee 15 December 2010
- Paper on the possible costs of wider use of PCV13

Agenda item 9:

- WHO position paper on polio vaccines and polio immunisation in the pre-eradication era
- Options appraisal on polio vaccines for the control of poliovirus outbreaks

Agenda item 10:

- Paper responding to a JCVI call for evidence on ‘Infanrix penta + Menitorix‘ and ‘Infanrix hexa’

Agenda item 11:

- Paper and publications on the GRADE system

Agenda item 12:

- Publication on automimmune/inflammatory syndrome induced by adjuvants
- Letter on inclusion of myagic encephalomyelitis in the seasonal influenza vaccination programme
- Consultation document on a new value-based approach to the pricing of branded medicines