JCVI statement on the annual influenza vaccination programme – extension of the programme to children
25 July 2012

Background

1. In 2011, the Secretary of State for Health asked JCVI to consider and make recommendations on possible extensions to the influenza vaccination programme to include the routine vaccination of a range of age groups of the healthy population. The current public vaccination programme is based on a risk approach with annual vaccination being recommended for those aged 65 years and over and those in the defined influenza clinical risk groups including all pregnant women.

2. During 2011, JCVI reviewed an unpublished study[1,2,3] from the Health Protection Agency (HPA) and London School of Hygiene and Tropical Medicine (LSHTM) on the impact and cost effectiveness of the current influenza vaccination programme and a range of possible extensions to the programme to low risk groups (i.e. to include people without clinical risk factors for influenza in various age groups). The study estimated the impact (numbers of influenza-related GP consultations, hospitalisations and deaths) and the incremental cost effectiveness of a range of extended influenza vaccination programmes compared with the current influenza vaccination programme in England based on reconstructions of influenza seasons from 1995/6 to 2008/9. The running costs of the current and extended programme were based on estimated vaccine and vaccine administration costs (initial costs to introduce the current or an extended programme were not considered). The assessment of cost effectiveness followed the methodology and criteria of the National Institute of Health and Clinical Excellence. The study was peer-reviewed in September 2011 by the JCVI influenza sub-committee augmented by additional experts in infectious disease mathematical modelling and health economics[4] before being considered by JCVI in October 2011[5].

3. Following consideration of the study, JCVI issued a position statement in November 2011[6] noting that the study suggested that the current influenza vaccination programme is highly likely to be cost effective, particularly when considered over a number of years. The study also suggested that extending the programme to low risk children is likely to be cost effective as this could both provide direct protection lowering the impact of influenza on children and indirect protection lowering influenza transmission from children to other children, adults and those in the clinical risk groups of any age.

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[1] Cromer *et al.* Estimating the burden of influenza by risk group. *Unpublished.*
[2] Baguelin *et al.* Reconstructing past influenza epidemics from consultation, virological surveillance data and a contact survey. *Unpublished.*
[3] Baguelin *et al.* The cost effectiveness of vaccination against seasonal influenza in England. *Unpublished.*
[4] JCVI influenza sub-committee meeting minute of September 2011: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_131105.pdf
[5] JCVI meeting minute of October 2011: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_133598.pdf
[6] JCVI statement on its position on the annual influenza vaccination programme. 16 November 2011 http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_131106.pdf

However, extending the influenza vaccination programme to all adults aged 50 to less than 65 years is unlikely to be cost effective and extending the programme to this or to other age groups in addition to low risk children would provide little additional benefit. Whilst JCVI agreed in principle to support extension of the vaccination programme to low risk children on the basis of the findings of the study, the committee asked for a range of further information, including additional analyses, before it could come to firm conclusions and make recommendations.

4. The additional information was reviewed by JCVI in April and June 2012[7]. This included: (i) an update to the HPA-LSHTM cost effectiveness study to include additional analyses that had been reviewed by members of the JCVI influenza sub-committee and additional experts and an analysis to estimate the cost effectiveness of extending the programme to children aged two to less than 17 years; (ii) a summary of published studies on the contribution of children to influenza transmission and evidence of indirect protection from influenza vaccination of children; (iii) further information on the effectiveness, safety and supply of a live attenuated intranasal influenza vaccine; (iv) the findings of qualitative research on the attitudes of parents, children, teachers and healthcare professionals to an influenza vaccination programme for children; (v) an analysis of the resources needed to implement a schools-based influenza vaccination programme and (vi) an analysis of the cost effectiveness envelope based on the HPA-LSHTM study to assess what the limits on start-up costs may be on an extended programme.

Consideration of the evidence

5. JCVI considered that the updated cost effectiveness study was well conducted, was based on appropriate and accepted methodology and had included reasonable assumptions. The study therefore provided a suitable and robust basis for informing immunisation policy, although there are uncertainties about some key parameters (e.g. indirect protection, vaccine uptake). The study suggested that, despite the high cost, extending the influenza vaccination programme to low risk children is highly likely to be cost effective and well below the established cost effectiveness threshold when indirect protection to the whole population is taken into account, particularly over the longer-term. Extending vaccination to low risk children aged five to less than 17 years was the most cost effective option evaluated. Vaccinating low risk children aged six months to less than 17 years is also likely to be cost effective, although the additional benefit from vaccinating the six months to less than five years age group is relatively small compared with that arising from vaccinating children aged five to less than 17 years. It also assumed high effectiveness of influenza vaccination in younger children, which is uncertain for most influenza vaccines. The study suggested that over the range of uptake of vaccine by children (aged six months to less than 17 years or five to less than 17 years) that had been assumed (15-50%), the extended programme might appreciably lower the public health impact of influenza by averting a large number of cases of influenza disease in children as well as many cases of severe influenza disease and influenza-related deaths, which mostly occur in older adults and those of any age with clinical risk factors. However, there is uncertainty about the level of expected population impact arising from the vaccination of children. Whilst most published

[7] JCVI meeting minutes of April and June 2012 available at: http://www.dh.gov.uk/ab/JCVI/DH_132441

studies looking at indirect protection from influenza vaccination of children suggest that a population impact should be expected, the approaches used and the quality of the studies and the magnitude of effect observed varied. The cost effectiveness study also suggested that extending influenza vaccination to children remained cost effective in circumstances where vaccine uptake by clinical risk groups was substantially increased. If vaccine uptake is increased in clinical risk groups that in itself is also likely to be cost effective. There would be relatively little further benefit from extending the vaccination programme to adult age groups of the low risk population in addition to low risk children and that is unlikely to be cost effective.

6. JCVI noted that research suggested that public attitudes to annual influenza vaccination of children may vary considerably because of doubts about the perceived risks posed to healthy children by influenza and about the need to protect healthy children from influenza.

7. JCVI noted that there is evidence from the implementation of other immunisation programmes (e.g. HPV vaccination) that offering vaccination through schools can be the most effective route to deliver immunisations to school-aged children. In addition, attitudinal research suggested that the mode of delivery of influenza vaccinations through schools may be generally well accepted. However, an analysis suggested that currently there are far too few school nurses to allow the implementation of a programme by this route, which would require very intense activity over a period of about two months each Autumn to deliver vaccinations ahead of the influenza season. Even to achieve relatively modest levels of uptake, the provision of school nursing services would need to be expanded very considerably (several-fold), at least over this two month period, or alternative arrangements investigated such that other appropriate persons might administer the vaccination. Furthermore, current changes to the education system with increasing numbers of schools becoming academies, and therefore outside of local authority control, may present additional challenges to the implementation of a schools-based programme. It would be for academies to decide on an individual basis whether to accept or reject the delivery of the programme in school.

8. JCVI noted that there is evidence that the authorised live attenuated intranasal influenza vaccine (Fluenz® marketed by AstraZeneca) is more effective compared with inactivated influenza vaccines in children aged six to 17 years (mean age 11 years)[8] as well as in younger children[9,10,11,12] and may offer protection against drifted strains. The vaccine

[8] Fleming *et al.* (2006) Comparison of the efficacy and safety of live attenuated cold-adapted influenza vaccine, trivalent, with trivalent inactivated influenza virus vaccine in children and adolescents with asthma. *Pediatr. Infect. Dis. J.* 25, 860-869.

[9]Vesikari *et al.* (2006) Safety, efficacy, and effectiveness of cold-adapted influenza vaccine-trivalent against community-acquired, culture-confirmed influenza in young children attending day care. *Pediatrics*. 118, 2298-312.

[10]Bracco *et al.* (2009) Efficacy and safety of 1 and 2 doses of live attenuated influenza vaccine in vaccine-naive children. *Pediatr Infect Dis J* 28, 365-71.

[11]Tam *et al.* (2007) Efficacy and safety of a live attenuated, cold-adapted influenza vaccine, trivalent against culture-confirmed influenza in young children in Asia. *Pediatr Infect Dis J* 26(7): 619-28.

[12]Belshe *et al.* (1998) The efficacy of live attenuated, cold-adapted, trivalent, intranasal influenza virus vaccine in children. *N Engl J Med* 338, 1405-12.

has a good safety profile in children aged two years and older and has an established history of use in the United States. It is authorised for use in children aged two to less than 18 years. However, it is not authorised for children aged less than two years and a small proportion of children (including those with compromised immune systems, severe asthma or severe egg allergy). JCVI noted a suggestion by its influenza sub-committee[4] that since this vaccine is comprised of whole virus, it may offer important longer-term immunological advantages to children by replicating natural exposure/infection to induce potentially better immune memory to influenza that may not arise from the annual use of inactivated vaccines. In addition, evidence from attitudinal research suggested that this vaccine, as it is administered by nasal spray, may be more widely accepted by parents of school-aged children and school-aged children themselves compared with injected influenza vaccines. However, there may be some parental concern about the reaction from the youngest school-age and pre-school children to the nasal spray. Information from the manufacturer suggested that sufficient supplies of vaccine could be provided given a sufficiently long lead-in time.

Recommendations

9. On the basis of the findings of the cost effectiveness study and the committee's previous conclusions[6], JCVI recommends that the annual influenza vaccination programme be extended to include school-aged children (spanning ages five to less than 17 years) as this is highly likely to be cost effective and well within accepted cost effectiveness thresholds. It is the most cost effective option evaluated. Extending the vaccination programme to include low risk children aged six months to less than five years as well as aged five to less than 17 years is also likely to be cost effective, although the additional benefit may be relatively small in comparison. However, JCVI is not in a position to recommend inclusion of all low risk children aged six months to less than five years. This is because there is no demonstrably equivalently effective vaccine to the vaccine of choice (see below) available for children aged less than two years. The application for market authorisation of an adjuvanted inactivated influenza vaccine for use in children aged six months to less than nine years with equivalent effectiveness has been withdrawn[13] and the authorised alternative unadjuvanted inactivated influenza vaccines are of uncertain effectiveness in young children. In light of this situation, JCVI recommends that an extended influenza vaccination programme should include low risk children aged two to less than five years in addition to children aged five to less than 17 years. An analysis suggests that additionally vaccinating low risk children aged two to less than five years is also likely to be cost effective. However, attitudinal research suggests that the annual influenza vaccination of pre-school children may be less well accepted by parents than vaccination of school-aged children.

10. Extending vaccination beyond low risk children to age groups of low risk adults aged under 65 years is unlikely to be cost effective and is not recommended.

11. JCVI advises that the live attenuated intranasal influenza vaccine (Fluenz®) should be the vaccine of choice for the extension to the programme, given the evidence of

[13] European Medicines Agency. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002299/wapp/Initial_authorisation/human_wapp_000129.jsp&mid=WC0b01ac058001d128&murl=menus/medicines/medicines.jsp

effectiveness, protection against drifted strains and safety, and in the absence of any equivalently effective alternative authorised vaccine. There may also be longer-term immunological advantages to the use of a live attenuated influenza vaccine. However, arrangements should be made to offer alternative authorised vaccines for the small proportion of children for whom the live attenuated vaccine is not suitable as most will be in clinical risk groups and need direct protection against influenza.

12. JCVI considers that the extension to the influenza programme to children aged five to less than 17 years may be best delivered through schools. For the purposes of implementation this could include children in reception to school year 12 in England and equivalent school years in other UK nations. Influenza immunisation of pre-school children from two years of age will necessitate a different mode of delivery for example, through general practice.

13. JCVI considers that the implementation of the recommendation needs very careful planning and handling. Routine annual influenza vaccination of children would be a huge expansion of the childhood immunisation programme as a whole; more than doubling the number of vaccinations offered currently to children before they reach adulthood. New large-scale supply, storage and distribution arrangements for vaccine would be required to facilitate the programme. Furthermore, current resources are insufficient to deliver an expanded programme through established routes (e.g. school nursing services) and solutions would be needed before an expanded programme could be implemented. It would be very important to mitigate potential opportunity costs to the current national immunisation programme and vital that the introduction of the extended programme does not adversely affect the programme as a whole in terms of resources and public perceptions. Resources should not be removed from the current national immunisation programme to implement and deliver an expanded influenza vaccination programme. Additionally, it would be inadvisable to introduce such a large immunisation programme into the NHS until the large scale restructuring of the health and public health system in England has been completed and the new system is running smoothly.

14. As attitudinal research suggests there may be mixed reactions to extending influenza vaccination to children, JCVI recommends that a campaign to inform and educate parents, children, healthcare professionals and others about influenza, the live attenuated intranasal vaccine and the benefits of the extending the programme to children and to the wider population would be needed in advance of, and alongside, an extended vaccination programme for successful implementation. Consideration should also be given as to whether the programme could provide an opportunity for the introduction of other health and/or health promotion programmes in schools.

15. Therefore, given the need for an extensive information/education campaign, the development of a strategy to implement and adequately resource an extended programme, ensure the large-scale supply, storage and distribution of vaccine and to allow the impending changes to the health and public health system in England to be completed, JCVI suggests that any expanded programme cannot be implemented until autumn 2014 at the very earliest and it may be longer before it can be implemented.

16. As with all immunisation programmes, JCVI will keep its advice and recommendations under review in light of new information that may emerge. JCVI recommends that the impact and cost effectiveness of the influenza programme be reviewed within five years of the introduction of the extended programme to assess whether the expected impact of the vaccine and the extension to the programme has been realised and to inform possible adjustments to the programme. Data to allow this retrospective evaluation should be collected. The review should include assessment of new improved alternative influenza vaccines, especially if shown to be effective in young children.

17. Until the extension to the programme can be implemented, the committee recommends that the influenza vaccination programme should continue to target all those aged 65 years and older and those aged six months to below 65 years in the influenza clinical risk groups (including pregnant women) for whom the burden of influenza is greatest. Increases in vaccine uptake in clinical risk groups are likely to be cost effective and should remain a priority, particularly for the youngest age groups where influenza vaccine uptake is poorest.