Public Health England

Protecting and improving the nation's health

Summary of data to support the choice of influenza vaccination for adults in primary care

Quadrivalent influenza vaccines

Quadrivalent influenza vaccines (QIV) cover the two main influenza B strains and aim to improve the breadth of protection provided in seasons when the circulating influenza B strain is not well matched to the single strain contained in the traditional trivalent vaccine (TIV). As influenza B is relatively more common in children than older age groups, the main clinical advantage of these vaccines is in childhood. Because of this, those vaccines centrally purchased for the childhood programme in recent years have been quadrivalent preparations. The use of live attenuated quadrivalent vaccine (LAIV - Fluenz-tetra) in children will therefore protect the age group where the infection is most common, and also reduce circulation of influenza B across the whole population and thus indirectly protect them.

Several studies in other settings indicate that QIV is likely to be cost effective compared with the trivalent vaccine (Meir et al 2015., Thommes et al 2015). Modelling by PHE has been conducted to understand the benefit of QIV in adults in the presence of the UK childhood programme. The model suggests that, once the programme in children of primary school age is fully established, there is still some benefit from using QIV in at risk adults under 65 years of age, including pregnant women. The model confirms, however, that there are relatively small additional health benefits to be gained by the use of QIV in older people. (Thorrington et al., 2017 – see table 1).

Table 1– Incremental benefit for each proposed QIV based vaccination programme: mean reduction in burden (adapted from Thorrington et al)

	Programme 1	Programme 2	Programme 3
Parameter	**Mean reduction after switching to QIV in children aged 2-11 years (SD)**	**Mean reduction after switching to QIV in 11-65 year olds on top of programme 1 (SD)**	**Mean reduction after switching to QIV in over 65 year olds on top of programme 2 (SD)**
Infections	643,652 (110,710)	136,284 (21,246)	39,297 (16,105)
Symptomatic cases	59,457 (20,816)	12,578 (4,264)	3,641 (1,942)
GP consultations	63,276 (10,680)	11,305 (1,757)	2,658 (1,123)
Hospitalisations	356 (64)	49 (9)	14 (6)

PHE publications gateway number: 2018696
Published: January 2018

Adjuvanted influenza vaccines

There is increasing evidence of the poor performance of non-adjuvanted, standard influenza vaccines in older people. A meta-analysis of data between 2004 and 2015 did not show any significant efficacy for the inactivated influenza vaccine in the elderly against the A(H3N2) influenza virus (Bellongia et al., 2016). This influenza sub-type is associated with significant impact in older people typically resulting in excess mortality and causing outbreaks in often highly vaccinated residents in care homes. PHE have also conducted an age stratified VE analysis of pooled primary care data since 2010/11 (submitted for publication). This showed significant effectiveness in the 65-74 age group for all influenza, for A(H1N1)pdm09,and for influenza B but no evidence of significant protection against A(H3N2). Above the age of 75 years, pooled estimates were unable to demonstrate any significant effectiveness across all seasons against influenza.
In response to the limited effectiveness of standard vaccines in older people, some pharmaceutical companies have been developing vaccines that lead to a better immune response in this group. An adjuvanted trivalent inactivated influenza vaccine (aTIV) Fluad® is now licensed for use in those aged 65 years and older in the UK. The aTIV has been licensed in some countries in Europe since 1997 and in the USA since 2015. Published data indicates that the adjuvanted vaccine has higher vaccine immunogenicity and higher effectiveness than non-adjuvanted vaccines in the elderly (Van Buynder et al, Vaccine 2013, Dominich et al., 2017).

Mathematical modelling by PHE indicates that, even under quite conservative estimates of effectiveness, the adjuvanted vaccine would be highly cost-effective in both the 65-74 and 75 year and over age groups with large reductions in GP consultations and hospitalisations (table 2). Given the low influenza vaccine effectiveness seen in the over 65 year olds in seasons dominated by A(H3N2), the JCVI agreed that use of aTIV in those aged 65 years and over would be both more effective and cost-effective than the non-adjuvanted vaccines currently in use. The priority for adjuvanted vaccine should be for those aged 75 years and above as this age group appear to derive little benefit from the standard vaccine (JCVI, October 2017). The vaccine would, however, also be effective and cost-effective in 65-74 year olds. Given the evidence above about the potential benefits of QIV, trivalent adjuvanted vaccine is a more appropriate choice than standard quadrivalent vaccine for older people.

Table 2: Incremental benefit of adjuvanted influenza vaccine targeting 75 years and above, compared to the current programme, and then adding adjuvanted vaccine for 65-74 year olds (Thorrington et al)

	Mean annual reduction (95% CI)	
Outcome	**TIV-adj for 75+ Compared to TIV baseline**	**TIV adj for 65+ Compared to TIV adj for 75+**
GP consultations	12,660 (12,012-13,305)	18,927 (18,240 – 19,616)
Hospitalisations	908 (872 – 944)	1,177 (1,142 – 1,211)
Flu attributable deaths	311 (296 – 325)	390 (376 – 403)

Summary

Based on the existing evidence, and in the context of the UK programme, PHE analysis strongly supports the preferential use of adjuvanted trivalent vaccine in older people. Based on current list prices for adjuvanted and standard vaccines, such a programme is likely to be highly cost effective. As advised by JCVI, the priority for 2018/19 should be those over 75 years of age, as this group are likely to derive very limited benefit from the existing programme.

Although quadrivalent vaccine offers the potential to provide broader direct protection against influenza B, the existence of a successful childhood programme using quadrivalent LAIV is likely to offer indirect protection by reducing transmission. On top of the childhood programme, the benefits of QIV in older people are limited. The priority groups where QIV should still be considered are therefore adult at-risk-groups, including pregnant women. Although formal analysis of the benefit of QIV in healthcare workers has not been conducted, this group are also likely to derive some benefit in those years when the circulating influenza B strain is not well matched to the B strain in TIV.

Published: January 2018

PHE supports the UN Sustainable Development Goals