

Joint Committee on Vaccination and Immunisation

Advice on influenza vaccines for 2022/23

September 2021

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Joint Committee on Vaccination and Immunisation

Advice on influenza vaccines for 2022/23

Prepared by the Joint Committee on Vaccination and Immunisation scientific secretariat

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JCVI advice on influenza vaccines for the 2022/2023 influenza season

JCVI has reviewed the latest evidence on influenza vaccines. The advice below represents the JCVI's scientific view on the use of influenza vaccines in the UK for the 2022/2023 influenza season.

Adults 65 years of age and over

For vaccination of those aged 65 years and over JCVI advises the use of the following vaccines:

- Adjuvanted quadrivalent inactivated influenza vaccine (aQIV)
- High-dose quadrivalent inactivated influenza vaccine (QIV-HD)
- Quadrivalent Recombinant Influenza Vaccine (QIVr)

Considerations

The available evidence indicates additional benefit from the use of aQIV or QIV-HD in those aged 65 years and over, compared with standard dose egg-culture inactivated trivalent and quadrivalent vaccines (TIVe/QIVe).

When considering a preference between QIV-HD and aQIV, the available data comparing these are few, somewhat inconsistent, are not available over multiple seasons, are at risk of bias, and are limited by the use of non-laboratory confirmed influenza endpoints. The level of uncertainty in the available evidence is considered too great to allow for a preferential recommendation between the vaccines.

The Committee is also of the view that there is enough supporting evidence for QIVr to be considered as equivalent to aQIV and QIV HD for use in those aged 65 years and older. This evidence includes that QIVr has a higher antigen content (45 µg) than QIVc (15 µg) and standard egg based quadrivalent vaccines (15 µg), as well as immunogenicity, efficacy and effectiveness data in favour of its use in the elderly alongside aQIV and QIV HD.

If aQIV, QIV-HD or QIVr are not available, the quadrivalent influenza cell-culture vaccine (QIVc) is considered an acceptable alternative and is suitable for use in this age group. QIVc is preferable to the standard egg-culture influenza vaccines (TIVe/QIVe) in this age group.

At-risk adults (including pregnant women) aged less than 65 years of age*

For vaccination of adults aged 18 to less than 65 years of age in an at-risk group JCVI advises the use of the influenza vaccines below:

- Quadrivalent influenza cell-culture vaccine (QIVc)
- Quadrivalent Recombinant Influenza Vaccine (QIVr)

The Quadrivalent influenza egg-culture vaccine (QIVe) can also be considered for use in this age group if other options are not available subject to the considerations below.

Considerations

Evidence from recent influenza seasons indicate a clear additional benefit in the use of quadrivalent influenza vaccines in those less than 65 years of age in an at-risk group, compared with trivalent influenza vaccines.

There is a potential advantage to using influenza vaccines which do not use eggs in the manufacturing process (cell-culture or recombinant) compared with egg-cultured influenza vaccines, due to the possible impact of “egg-adaptation” on the effectiveness of influenza vaccines, particularly against A(H3N2) strains. The evidence on additional benefit is available for only very few seasons but the issue of egg adaptation remains a real concern particularly for the AH3N2 virus which is the more virulent influenza subtype in terms of morbidity and mortality.

There is limited but good evidence that the recombinant vaccine QIVr, which also is not affected by egg adaptation, is more effective than QIVe in adults under 65 years age. Therefore, QIVr is also preferred over QIVe in adults under 65 years old.

Based on the available evidence the Committee supports a preference for QIVc and QIVr over QIVe. The quadrivalent egg-culture inactivated vaccine (QIVe) can also be considered for use in this group, if other options are not available, because any impact of egg adaptation will likely be limited to seasons in which the influenza season is dominated by well- matched H3N2 strains.

* This advice also applies to adults aged 50 to 64 years old who are not in a clinical risk group if the temporary enhanced influenza programme continues in 2022/23

Children aged two to less than 18 years of age in an at-risk group

Children aged two years to less than 18 years in clinical risk groups should be offered the live attenuated Influenza vaccine (LAIV) unless it is medically contraindicated or otherwise unsuitable. In those for whom LAIV is not suitable, JCVI advises the use of QIVc. JCVI therefore advises the influenza vaccines below in the following order of preference:

1. live attenuated Influenza vaccine (LAIV)
2. Quadrivalent influenza cell-culture vaccine (QIVc)¹

The Quadrivalent influenza egg-culture vaccine (QIVe) can also be considered for use in this age group if other options are not available.

Children aged less two years old

For vaccination of at-risk children aged less than 2 years of age in an at-risk group JCVI advises the use of the following vaccine:

- Quadrivalent influenza egg-culture vaccine (QIVe)²

The Committee has also advised that Egg-allergic children aged less than two years can also be offered the quadrivalent inactivated egg-free vaccine, QIVc (Flucelvax® TETRA). This is an off-label recommendation which is supported by unpublished data which shows non inferiority immunogenicity and a very similar safety profile for QIVc compared with QIVe in children less than two years old.

Generating real world evidence in the UK

Further comparative data are required, preferably from the same country over multiple seasons and with laboratory confirmed influenza endpoints, to support consideration of the relative effectiveness of the influenza vaccines available in the UK across the different age and risk groups in which they are licensed. The Committee would like to see high quality comparative data generated in the UK. Most of these data can potentially be generated from the monitoring and surveillance of vaccine effectiveness (VE) in primary and secondary care for those influenza vaccines delivered through the influenza vaccination programme.

The COVID-19 pandemic has provided much greater insight into the importance of virologically confirmed VE studies for hospitalisation and death, and the use of NHS data to drive this, and how the critical hospital admission clinical endpoint may give very divergent results from community-based VE testing. COVID19 has also shown the potential of real time data being available through improvements in NHS data linkage,

¹ The Quadrivalent influenza cell-culture vaccine (QIVc) is egg free and egg allergic individuals can be safely vaccinated in any setting with this vaccine, including those who have required admission to intensive care for a previous severe anaphylaxis to egg

² The quadrivalent influenza egg culture vaccine (QIVe) is the only available influenza vaccine licensed for use in children aged less than two years old

which now need to be applied to influenza. Therefore, the Committee would like to see the existing influenza surveillance system for generating influenza VE enhanced to generate adequately powered data to inform future JCVI decisions and advice which will benefit public health in the longer term. The Committee agrees that enhancing the existing surveillance system is critical to ensure the UK population receives the best possible clinical benefit from the available influenza vaccines. This should form part of the longer-term planning for a first class influenza programmes as a whole alongside other research initiatives

Other research initiatives could also contribute to improving evaluation of influenza vaccines in the UK and the Committee notes the close working of industry, regulators, government and public funded research behind the rapid introduction and real-time evaluation of COVID-19 vaccines and would support similar initiatives applied to evaluating Influenza vaccines.

The Committee would like to see all the available vaccines which it has advised in preference to standard egg-based vaccines used in the UK so they can be properly evaluated through the programme but understands that this is subject to NHS negotiations (see below). There might be important differences in the products which could lead to a differential impact on winter pressures, and it would be difficult to evaluate the significance of this for the NHS unless all the advised products are available in the programme.

Operational considerations

The Committee is mindful that factors other than purely scientific and clinical advice need to be considered from an operational perspective, which include availability of supply and affordability, which will contribute to the decisions on which vaccines are purchased for the 2022/23 season. The aim of this advice is to provide a framework from which NHS England and PHE[†] can take forward planning for the delivery of the Influenza programme in 2022/23 and communicate this clearly to providers and the public.

Background

The considerations of JCVI with regards to use of these vaccines are published in the minutes of JCVI and the Influenza sub-committee

The advice of JCVI is based on discussions at JCVI and the Influenza sub-committee:

1. adjuvanted influenza vaccines were discussed in the June and October 2017 JCVI meetings, and the September 2019 Influenza sub-committee;
2. high dose influenza vaccines were discussed in the June 2018 JCVI meeting, the September 2018 Influenza sub-committee, and the September 2019 Influenza sub-committee;

3. cell-culture vaccines were discussed in the September 2018 Influenza sub-committee meeting, the October 2018 JCVI meeting, and the September 2019 Influenza sub-committee;
4. advice for the 2021/22 season was discussed via teleconference with the JCVI and invited experts from influenza subcommittee on 27 October 2020. The minutes of this meeting were published on the 8 December 2020.
5. Advice for the 2022/23 season was discussed via teleconference with the JCVI Influenza subcommittee on 3 September 2021 and subsequently ratified by the main JCVI Committee via correspondence. The minutes of the subcommittee will be published within six weeks of the next routine JCVI meeting.

The minutes of JCVI and sub-committee meetings are available through the JCVI webpage at <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation>

Glossary

aQIV - Adjuvanted egg-cultured quadrivalent inactivated influenza vaccine

LAIV - Live attenuated egg-cultured intranasal influenza vaccine

QIVc - Cell-cultured quadrivalent inactivated influenza vaccine

QIVe - Egg-cultured quadrivalent inactivated influenza vaccine

QIVr – Recombinant quadrivalent inactivated influenza vaccine

TIVe - Egg-cultured trivalent inactivated influenza vaccine

QIV-HD - High-dose egg-cultured quadrivalent inactivated influenza vaccine

Selected references

- Bella *et al* (2019) Effectiveness of the trivalent MF59 adjuvated influenza vaccine in preventing hospitalization due to influenza B and A(H1N1)pdm09 viruses in the elderly in Italy, 2017 - 2018 season. *Expert Rev Vaccines*. 2019 Jun;18(6):671-679.
- Boikos C, Sylvester GC, Sampalis JS, Mansi JA. Relative Effectiveness of the Cell-Cultured Quadrivalent Influenza Vaccine Compared to Standard, Egg-Derived Quadrivalent Influenza Vaccines in Preventing Influenza-Like Illness in 2017-2018. *Clinical infectious diseases* 2020; Apr 7:ciaa371. doi: 10.1093/cid/ciaa371.
- Boikos C, Imran M, Nguyen VH, Ducruet T *et al*. Effectiveness of the Cell-Derived Inactivated Quadrivalent Influenza Vaccine in Individuals at High Risk of Influenza Complications in the 2018-2019 United States Influenza Season. *Open Forum Infect Dis*. 2021 Apr 2;8(7):ofab167. doi: 10.1093/ofid/ofab167.
- Bruxvoort KJ, Luo Y, Ackerson B, et al. Comparison of vaccine effectiveness against influenza hospitalization of cell-based and egg-based influenza vaccines, 2017-2018. *Vaccine* 2019; 37(39): 5807-11.
- Dawood FS, Naleway AL, Flannery B *et al*. Comparison of the Immunogenicity of Cell Culture-Based and Recombinant Quadrivalent Influenza Vaccines to Conventional Egg-Based Quadrivalent Influenza Vaccines Among Healthcare Personnel Aged 18–64 Years: A Randomized Open-Label Trial. *Clin Infect Dis*. 2021 Jul 10:ciab566. doi: 10.1093/cid/ciab566. Epub ahead of print.
- DiazGranados *et al* (2014) Efficacy of high-dose versus standard-dose influenza vaccine in older adults. *N Engl J Med*; 371: 635–45.
- Divino *et al* (2019) Real-World outcomes of adjuvanted trivalent Influenza vaccine compared to egg-based trivalent high-dose, egg-based quadrivalent and trivalent vaccines among the U.S. elderly during 2016-2018 Flu seasons using Claims Data. Poster Presented at OPTION X Congress; August 31st 2019, Singapore.
- Divino *et al* (2019) Hospitalization encounters following vaccination with adjuvanted trivalent Influenza vaccine compared to egg-based trivalent high-dose, egg-based quadrivalent and trivalent vaccines among the U.S. elderly using claims data. Poster Presented at OPTION X Congress; August 31st 2019, Singapore.
- Divino V et al. A real-world study evaluating the relative vaccine effectiveness of a cell based quadrivalent influenza vaccine compared to egg-based quadrivalent influenza vaccine in the US during the 2017–18 influenza season. *Vaccine* 2020; 38: 6334–6343.
- Dunkle LM, Izikson R, Patriarca P, Goldenthal KL, Muse D, Callahan J, et al. Efficacy of recombinant influenza vaccine in adults 50 years of age or older. *New England Journal of Medicine*. 2017;376(25):2427-36.
- Dunkle LM, Izikson R, Patriarca PA, Goldenthal KL, Muse D, Cox MMJ. Randomized Comparison of Immunogenicity and Safety of Quadrivalent Recombinant Versus Inactivated Influenza Vaccine in Healthy Adults 18-49 Years of Age. *J Infect Dis*. 2017 Dec 5;216(10):1219-1226. doi: 10.1093/infdis/jix478. PMID: 28968871.
- Eichelberger MC, Wan H. Influenza neuraminidase as a vaccine antigen. *Curr Top Microbiol Immunol*. 2015;386:275-99. doi: 10.1007/82_2014_398. PMID: 25033754. 6)

Eick-Cost AA. Relative effectiveness of cell-based influenza vaccines compared with egg-based influenza vaccines, active component U.S. Service members, 2017–18 season International Conference on Emerging Infectious Diseases. Atlanta, GA.; 2018. Gravenstein *et al* (2017) Comparative effectiveness of high-dose versus standard-dose influenza vaccination on numbers of US nursing home residents admitted to hospital: a cluster-randomised trial. *Lancet Respir Med*. 2017 Sep;5(9):738-746.

European Centre for Disease Prevention and Control. Systematic review of the efficacy, effectiveness and safety of newer and enhanced seasonal influenza vaccines for the prevention of laboratory confirmed influenza in individuals aged 18 years and over. Stockholm: ECDC; 2020

Gravenstein *et al* (2018) Feasibility of a cluster-randomized influenza vaccination trial in U.S. nursing homes: Lessons learned. *Hum Vaccin Immunother*. 2018 Mar 4;14(3):736-743

Giurgea LT, Morens DM, Taubenberger JK *et al*. Influenza Neuraminidase: A Neglected Protein and Its Potential for a Better Influenza Vaccine. *Vaccines* 2020;8:409 doi.org/10.3390/vaccines8030409

Izurieta *et al* (2015) Comparative effectiveness of high-dose versus standard-dose influenza vaccines in US residents aged 65 years and older from 2012 to 2013 using Medicare data: a retrospective cohort analysis. *Lancet Infect Dis*. 2015 Mar;15(3):293-300

Izurieta *et al* (2019) Relative Effectiveness of Cell-Cultured and Egg-Based Influenza Vaccines Among Elderly Persons in the United States, 2017–2018. *J Infect Dis*. 2019 Sep 13;220(8):1255- 1264

Izurieta HS, Lu M , Kelman J *et al*. Relative effectiveness of influenza vaccines among the U.S. elderly, 2018-19. *J Infect Dis* 2020; 222:278–87. *Clin Infect Dis*. 2020 Nov 19:ciaa1727. doi: 10.1093/cid/ciaa1727. Epub ahead of print.

Izurieta HS, Chillarige Y, Kelman J, Wei Y, Lu Y Comparative effectiveness of influenza vaccines among U.S. Medicare beneficiaries ages 65 years and older during the 2019-20 season. *Clin Infect Dis*. 2020 Nov 19:ciaa1727. doi: 10.1093/cid/ciaa1727. Epub ahead of print.

Krammer F, Lei L, Wilson P Emerging from the Shadow of Hemagglutinin: Neuraminidase Is an Important Target for Influenza Vaccination. *Cell Host & Microbe* 2019; 26(6):712-713. :<https://doi.org/10.1016/j.chom.2019.11.006>.

Lapi *et al* (2019) Adjuvanted versus nonadjuvanted influenza vaccines and risk of hospitalizations for pneumonia and cerebro/cardiovascular events in the elderly. *Expert Rev Vaccines*. 2019; 18(6):663-670

Lee JKH, Lam GKL, Shin T *et al*. Efficacy and effectiveness of high-dose influenza vaccine in older adults by circulating strain and antigenic match: An updated systematic review and meta-analysis. *Vaccine*. 2021 Mar 15;39 Suppl 1:A24-A35. doi: 10.1016/j.vaccine.2020.09.004. Epub 2021 Jan 7.

Mannino *et al* (2012) Effectiveness of Adjuvanted Influenza Vaccination in Elderly Subjects in Northern Italy. *American Journal of Epidemiology*. 176(6) 527–533

Maryna C Eichelberger, Arnold S Monto, Neuraminidase, the Forgotten Surface Antigen, Emerges as an Influenza Vaccine Target for Broadened Protection, *The Journal of Infectious Diseases*, Volume 219, Issue Supplement_1, 15 April 2019, Pages S75–S80, <https://doi.org/10.1093/infdis/jiz017>

Pelton SI, Divino V, Shah D *et al*. Evaluating the Relative Vaccine Effectiveness of Adjuvanted Trivalent Influenza Vaccine Compared to High-Dose Trivalent and Other Egg-Based Influenza Vaccines among Older Adults in the US during the 2017–2018 Influenza Season. *Vaccines* 2020, 8, 446

Rijal, Pramila & Wang, Bei & Tan, Tiong & Schimanski, Lisa & Janesch, Philipp & Dong, Tao & McCauley, John & Daniels, Rodney & Townsend, Alain & Huang, Kuan-Ying. (2019). Broadly inhibiting

anti-neuraminidase monoclonal antibodies induced by trivalent influenza vaccine and H7N9 infection in humans. 10.1101/682450. 5)

Robison & Thomas (2018) Assessing the effectiveness of high-dose influenza vaccine in preventing hospitalization among seniors, and observations on the limitations of effectiveness study design. *Vaccine*. 2018 Oct 29;36(45):6683-6687

Treanor JJ, El Sahly H, King J, Graham I, Izikson R, Kohberger R, et al. Protective efficacy of a trivalent recombinant hemagglutinin protein vaccine (FluBlok®) against influenza in healthy adults: a randomized, placebo-controlled trial. *Vaccine*. 2011;29(44):7733-9.

van Aalst R, Gravenstein S, Mor V, Mahmud SM, Wilschut J, Postma M, Chit A. Comparative effectiveness of high dose versus adjuvanted influenza vaccine: A retrospective cohort study. *Vaccine*. 2020 Jan 10;38(2):372-379. doi: 10.1016/j.vaccine.2019.09.105. Epub 2019 Oct 9. PMID: 31606249.

Van Buynder *et al* (2013) The comparative effectiveness of adjuvanted and unadjuvanted trivalent inactivated influenza vaccine (TIV) in the elderly. *Vaccine*. 31(51) 6122-6128

Young-Xu *et al* (2018) Relative Vaccine Effectiveness of High-Dose Versus Standard-Dose Influenza Vaccines Among Veterans Health Administration Patients. *J Infect Dis*. 217, 11, 1718–1727

Young-Xu *et al* (2019) Analysis of relative effectiveness of high-dose versus standard-dose influenza vaccines using an instrumental variable method. *Vaccine* 37(11) 1484-1490

† From October 2021, these responsibilities will be transferred from PHE to the newly established UK Health Security Agency (UKHSA)