National Immunisation Advisory Committee

UPDATED RECOMMENDATIONS FOR THE USE OF COVID-19 VACCINES

NIAC | 10.03.2021

Request for National Immunisation Advisory Committee advice

On 4 March 2021, the National Immunisation Advisory Committee (NIAC) was asked to consider any new evidence relating to the use of COVID-19 vaccines in particular groups and to provide advice in respect of the use of COVID-19 vaccines in Ireland.

Background

NIAC previously provided recommendations to the Department of Health related to COVID-19 vaccination:

- COVID-19 Vaccine AstraZeneca in those aged 70 years and older, February 2021
- COVID-19 vaccination in those aged 65-69 years, February 2021
- Recommendations for COVID-19 vaccine prioritisation, February 2021

The risk of a severe outcome from COVID-19 is correlated with increasing age. All three authorised vaccines currently available in Ireland are very efficacious in preventing hospitalisations and severe COVID-19 disease, which is the primary aim of the vaccination programme. Overall efficacy* in preventing all PCR positive symptomatic COVID-19 is higher in the mRNA COVID-19 vaccines (COVID-19 Vaccine Moderna®, Comirnaty® BioNTech/Pfizer), when used in the recommended 2 dose schedule, than in the authorised viral vector COVID-19 Vaccine Astra Zeneca®.

The European Medicines Agency authorised the COVID-19 Vaccine AstraZeneca® for use in all adults aged 18 years and older, including those aged 65 and older. The overall efficacy was reported as 59.5% but there were insufficient clinical data in those aged 55 and older to allow reliable calculation of efficacy. However, as a similar immune response was shown in all age groups, including those 65 years and older, it was expected that the COVID-19 Vaccine AstraZeneca® will be effective in this age group.

On 10 February 2021, the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) reported the overall efficacy of COVID-19 Vaccine AstraZeneca® at 63.1%. Although the group of those less than 65 years was too small to assess protection based on the efficacy data alone, the immunogenicity data did not differ by age cohort.

WHO recommended COVID-19 Vaccine AstraZeneca® for use in persons aged 65 years and older.

NIAC reviewed new evidence published since the recommendations noted above, that might warrant a change to current advice.

***Efficacy** is the degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled circumstances i.e. in a randomised controlled clinical trial.

***Effectiveness** refers to how well the vaccine performs in the real world. Although a vaccine that has high efficacy would be expected to be highly effective in the real world, it is unlikely to be exactly the same.

New evidence

The relevant new evidence relates to the real-world effectiveness of COVID-19 Vaccine AstraZeneca® in those aged 65 years and older, as outlined in Table 1.

Table 1. Effectiveness of COVID-19 Vaccine AstraZeneca® (ChAdOx1) in those aged 65 years and older

References	Study	Results	Conclusion
Hyams et al. (Posted: 3 Mar 2021) **Assessing the effectiveness of BNT162b2* and ChAdOx1nCoV-19* COVID-19 vaccination in prevention of hospitalisations in elderly and frail adults: a single centre test negative case-control study** (preprint available at https://ssrn.com/abstract=3796835 accessed 05.03.2021)	Prospective single-centre test-negative design case-control study of adults aged ≥80 years hospitalised with COVID-19 disease or other acute respiratory disease 803 individuals >80yrs hospitalised with respiratory disease Study period 18th Dec to 26th Feb	First dose vaccine effectiveness (VE) of BNT162b2 was 71.4% (95% confidence interval [CI] 46.5-90.6) and for ChAdOx1nCoV-19 was 80.4% (95% CI 36.4-94.5). When effectiveness analysis for BNT162b2 was restricted to the period covered by ChAdOx1nCoV-19, the estimate was 79.3% (95% CI 47.0-92.5. VE following 2 doses of BNT162b2 was 85-90%. 9 of the 36 cases 260(25%) with SARS-CoV-2 infection and 53 of 90 controls (58·9%) received one dose ChAdOx1nCoV-19 (difference, - 33.9% giving an unadjusted effectiveness of 76.7% (95% CI 46.5-90.6) and an adjusted effectiveness of 80.4% (36.4-94.5). Matched conditional sensitivity analysis again generated a slightly lower estimate with wider confidence	A single dose of either BNT162b2 or ChAdOx1nCoV-19 vaccine resulted in substantial reductions in the risk of COVID-19-related hospitalisation in elderly, frail patients with extensive co-morbid disease. *Caveats:* *Small number of ChAdOxt1 recipients with limited duration of follow up* *ChAdOx1 recipients N=62* *BNT162b2 recipients N=108*

		intervals which crossed zero. The apparent effectiveness up to 14 days was close to zero (OR 1.126) suggesting limited bias was present in the cohort.	
Lopez Bernal et al. (Posted March 02, 2021.) **Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in England** (preprint available at https://doi.org/10.1101/2021.03.01.21252652 accessed 05.03.2021)	Test negative case control design study to estimate the real-world effectiveness of the Pfizer/BioNTech BNT162b2 vaccine and AstraZeneca ChAdOx1 vaccine against confirmed COVID-19, hospitalisations and deaths in all adults in England aged 70 years and over (over 7.5 million) between 8th December 2020 and 19th February 2021.	With the ChAdOx1 vaccine, vaccine effects were seen from 14-20 days after vaccination reaching an effectiveness of 60% (95% CI 41-73%) from 28-34 days and further increasing to 73% (95% CI 27-90%) from day 35 onwards.	Vaccination with a single dose of ChAdOx1 COVI D-19 vaccination was associated with a significant reduction in symptomatic infection and severe disease. Protection was maintained for the duration of follow-up (>6 weeks). *Note:* *Number tested after 28 days was small. Maximum follow up after ChAdOx1 was 41 days. Second doses of ChAdOx1 have not yet been rolled out in England.*
Vasileiou et al. (Posted: 19 Feb 2021) **Effectiveness of first dose of COVID-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people** (preprint available at https://ssrn.com/abstract=3789264 accessed 05.03.2021)	Open, real-time prospective observational cohort study to examine the effectiveness of the first dose Pfizer-BioNTech (BNT162b2) and Oxford-AstraZeneca® (ChAdOx1) using hospitalisation and mortality records for 5.4 million people in Scotland. 37% of the cohort were aged 65 and over. Study duration 8th Dec – Feb 15th.	A statistically significant adjusted VE was found against COVID-19 related hospital admissions up to 34 days after the first dose of ChAdOx1 vaccination The first dose of the ChAdOx1 vaccine was associated with a vaccine effect v. hospitalisation Day 7-13: 70% (95%CI 63 to 76) Day 14-20: 74% (95%CI 66-81) Day 21 – 27: 85% (95%CI 72-90) Day 28 – 34: 94% (95%CI 73-99)	Results of combined effect of both vaccines for prevention of COVID-19 related hospitalisation were comparable in those aged ≥80 years (81%; 95% CI 65 to 90 at 28-34 days post-vaccination) *Note:* *Number estimated from graphic who were >70 years >300,000* *Maximum duration follow up for ChAdOx1=6 weeks*

*BNT162b2 refers to Pfizer-BioNtech Comirnaty® vaccine, ChAdOx1 refers to the COVID-19 Vaccine AstraZeneca®

Discussion

All three papers report on observational studies. Benefits of such studies include provision of additional information on characteristics of groups that may be under-represented in randomised controlled clinical trials e.g. persons 65 and older, those with comorbidities, immunosuppression due to disease or treatment, those on other medication and pregnancy. Limitations include: the timing of vaccination in relation to other public health measures such as lockdown, individual vaccine rollout and uptake, underlying changes in disease rates and limited duration of follow up.

The study limitations outlined above need to be considered in light of the significant strengths of well conducted population-based studies. The risks of recommending the COVID-19 Vaccine Astra Zeneca® when the follow up time in these effectiveness studies is limited are likely to be outweighed by the benefits of offering vaccination as soon as possible.

The COVID-19 Vaccine AstraZeneca® vaccine has shown significant effectiveness against hospitalisations and severe disease in those aged 65 years and over in post-marketing observational studies. The papers detailed above are preprints and have not yet been peer reviewed. However, vaccine effectiveness findings are consistent, with two of the three studies based on total population. Although the follow up period is short, effectiveness has not waned up to 6 - 8 weeks.

The time required for results of further studies must be offset by any delay in vaccination at this stage in the pandemic.

Recognising the importance of minimising vaccination delay, the additional data supports removal of the preferential recommendation for an mRNA vaccine in those aged 70 years and older. Any of the authorised vaccines can be used in this age group to effectively prevent COVID-19 related hospitalisation and severe disease.

The NIAC did not find any evidence regarding the effectiveness of COVID-19 vaccines in immunocompromised persons. The NIAC previously recommended the preferential use of mRNA vaccines for those aged 16-69 years with conditions that may limit COVID-19 vaccine immune response. This now applies to all those 16 years and older with these conditions.

Existing and updated recommendations

The impact of the above new evidence on existing NIAC recommendations is outlined below in Table 2.

Table 2. Summary of existing and updated NIAC COVID-19 vaccination recommendations

Existing recommendations	Updated recommendation 08 March 2021
Any currently authorised COVID-19 vaccine can be given to adults of all ages, including those aged 70 and older	Any currently authorised COVID-19 vaccine can be given to adults of all ages, including those aged 70 and older
Vaccination of those aged 70 and older should not be delayed. Where practicable and timely, those aged 70 and older should be given an mRNA vaccine.	
Where practicable and timely, those aged 16-69 years with conditions that may limit COVID-19 vaccine immune response should be given an mRNA vaccine	Where practicable and timely, those aged **16 years and older** with conditions that may limit COVID-19 vaccine immune response should be given an mRNA vaccine.
The two-dose COVID-19 Vaccine AstraZeneca® schedule should be administered at an interval of 8 - 12 weeks.	No change

Note: Those aged 16 and 17 years, for whom vaccination is recommended, should receive Comirnaty®/Pfizer BioNTech as the only COVID-19 vaccine authorised for use in this age group

These recommendations are based on current data and are subject to ongoing review.

DOH will be informed of any changes.